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# Acute kidney injury based on KDIGO (Kidney Disease Improving Global Outcomes) criteria in patients with elevated baseline serum creatinine undergoing cardiac surgery

Lesão renal aguda baseada nos critérios KDIGO (Kidney Disease: Improving Global Outcomes) em pacientes com creatinina sérica elevada submetidos à cirurgia cardíaca

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Abstract

Introduction: Preoperatively elevated serum creatinine (SCr) is considered an independent risk factor for morbidity and mortality after cardiac surgery. The aim of this study was to apply the Kidney Disease Improving Global Outcomes classification for acute kidney injury in a population of patients with preoperatively elevated serum creatinine who underwent cardiac surgery (coronary artery bypass grafting or cardiac valve surgery) and to evaluate the acute worsening of renal function as a predictor of 30-day mortality.

Methods: This was a single-center retrospective study that included patients from the Postoperative Cardiac Surgery Intensive Care Unit of the Hospital de Base, São José do Rio Preto Medical School. Demographics, type of surgery, laboratory data and pre, peri and postoperative data were obtained from a prospectively collected database. From January 2003 to June 2013, 2,878 patients underwent cardiac surgery, either coronary artery bypass grafting or cardiac valve surgery, at the Hospital de Base of São José do Rio Preto Medical School. Out of those, 918 showed elevated preoperative serum creatinine, with SCr > 1.30 mg/dL for men and > 1.00 mg/dL for women. Five hundred and forty nine patients (60%) undergoing coronary artery bypass grafting and 369 patients (40%) undergoing cardiac valve surgery. A Multivariate Cox Proportional Hazard Model (stepwise) was used to assess the relationship between AKI and mortality at 30 days.

Results: Out of the 918 patients studied, 391 (43%) had postoperative AKI: 318 (35%) had Kidney Disease Improving Global Outcomes stage 1, 27 (2.9%) had Kidney Disease Improving Global Outcomes stage 2, and 46 (5.0%) had Kidney Disease Improving Global Outcomes stage 3. Patients in every stage of acute kidney injury showed progressive increase in EuroSCORE values, 30-day mortality ratescardiopulmonary bypass duration, and intensive care length of stay. Among patients classified as Kidney Disease Improving Global Outcomes stage 3, 76% required dialysis with a 30-day mortality of 66%. The Cox proportional hazards model showed that the hazard ratio for 30-day mortality was 4.8 for Kidney Disease Improving Global Outcomes stage 1 patients, 13.5 for Kidney Disease Improving Global Outcomes stage 2 patients, and 20.8 for Kidney Disease Improving Global Outcomes stage 3 patients (P<0.001 for all). Subgroup analyses (coronary artery bypass grafting and cardiac valve surgery) had similar results.

Conclusion: In this population, acute kidney injury based on the Kidney Disease Improving Global Outcomes criteria was a powerful predictor of 30-day mortality in patients with elevated preoperative serum creatinine who underwent cardiac surgery (coronary artery bypass grafting or cardiac valve surgery).

Descriptors: Acute Kidney Injury. Creatinine. Cardiovascular Surgical Procedures. Hospital Mortality.

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This study was carried out in the Cardiac Intensive Care Unit from Hospital de Base, São José do Rio Preto Medical School, São José do Rio Preto, SP, Brazil.

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Abbreviations, acronyms & symbols			
ADQI	Acute Dialysis Quality Initiative		
AKI	Acute Kidney Injury		
AKIN	Acute Kidney Injury Network		
CABG	Coronary Artery Bypass Grafting		
CPB	Cardiopulmonary Bypass		
CVS	Cardiac Valve Surgery		
eGFR	Estimated Glomerular Filtration Rate		
HR	Hazard Ratio		
KDIGO	Kidney Disease Improving Global Outcomes		
OR	Odds Ratio		
RIFLE	Risk, Injury, Failure, Loss and End-stage Kidney		
	Disease		
SCr	Serum creatinine		

### Resumo

Introdução: Creatinina sérica (CSr) elevada no período pré-operatório é considerada um fator de risco independente para morbidade e mortalidade em cirurgia cardíaca. Avaliar o impacto da lesão renal aguda pelos critérios Kidney Disease Improving Global Outcomes como preditor de mortalidade em 30 dias em pacientes submetidos à revascularização miocárdica ou cirurgia valvar com creatinina sérica pré-operatória elevada.

Métodos: Este foi um estudo retrospectivo de centro único que incluiu pacientes da Unidade de Cuidados Intensivos em Pós-operatório de Cirurgia Cardíaca do Hospital de Base, Faculdade de Medicina de São José do Rio Preto. Dados demográficos, tipos de cirurgia, dados laboratoriais e informações pré, peri e pós-operatórias foram obtidos a partir de uma coleta prospectiva de banco de dados. Foram considerados 2878 pacientes consecutivamente submetidos à revascularização miocárdica ou cirurgia valvar no período de janeiro de 2003 a

junho de 2013. Destes, 918 indivíduos apresentavam creatinina sérica alterada no pré-operatório (CrS > 1.30 mg/dL para homens e > 1.00 mg/dL para mulheres), compreendendo 549 pacientes (60%) submetidos à revascularização miocárdica e 369 pacientes (40%) submetidos à cirurgia valvar. O modelo de riscos proporcionais de Cox foi utilizado para avaliar a relação entre lesão renal aguda e mortalidade em 30 dias.

Resultados: Nesta casuística, 391 pacientes (43%) apresentaram lesão renal aguda no pós-operatório, sendo 318 (35%) Kidney Disease Improving Global Outcomes estágio 1, 27 (2,9%) Kidney Disease Improving Global Outcomes estágio 2 e 46 (5.0%) Kidney Disease Improving Global Outcomes estágio 3. EuroSCORE, mortalidade em 30 dias, tempo de circulação extracorpórea e permanência em ambiente de terapia intensiva aumentaram progressivamente em todos os estágios. Dentre os pacientes classificados como Kidney Disease Improving Global Outcomes 3, 76% necessitaram diálise com mortalidade em 30 dias de 66%. A análise de Cox evidenciou razão de risco para óbito em 30 dias de 4,8 para pacientes Kidney Disease Improving Global Outcomes estágio 1, 13,5 para pacientes Kidney Disease Improving Global Outcomes estágio 2 e 20,8 para pacientes com Kidney Disease Improving Global Outcomes estágio 3 (P<0,001 para todos). Análise dos subgrupos (revascularização miocárdica e cirurgia valvar) obteve resultados semelhantes.

Conclusão: Lesão renal aguda pelos critérios Kidney Disease Improving Global Outcomes destaca-se como excelente preditor de óbito em 30 dias em indivíduos submetidos à revascularização miocárdica ou cirurgia valvar que apresentam creatinina sérica pré-operatória alterada.

Descritores: Lesão Renal Aguda. Creatinina. Procedimentos Cirúrgicos Cardiovasculares. Mortalidade Hospitalar.

### INTRODUCTION

As the population ages, more patients with renal dysfunction are being referred for cardiac surgery<sup>[1]</sup>. Elevated serum creatinine (SCr) preoperatively is considered an independent risk factor for morbidity and mortality after cardiac surgery<sup>[2,3]</sup>, with the overall risk of death for patients with creatinine ≥ 1.5 mg/dL ranging from 5% to 30%. Postoperatively, small changes in SCr, however small they may be, are also associated with a significant reduction in survival<sup>[4,5]</sup>. Elevated SCr may be associated with increased morbidity and mortality even when its change does not meet the criteria for acute kidney injury (AKI)<sup>[6]</sup>.

Several consensus definitions have been developed to provide uniform criteria for AKI diagnosis. In 2004, the "Acute Dialysis Quality Initiative (ADQI)" group proposed consensus guidelines and evidence-based treatment and prevention of AKI, which were later called the RIFLE criteria (Risk, Injury, Failure, Loss and End-stage Kidney Disease)<sup>[7]</sup>. The modification of these criteria was subsequently proposed by the "Acute Kidney Injury Network" (AKIN, which included the

ADQI group)<sup>[8-10]</sup>. More recently, the AKI study group "Kidney Disease: Improving Global Outcomes (KDIGO)" proposed a modified definition, combining the differences between the RIFLE and AKIN definitions<sup>[11]</sup> (Table 1).

The aim of this study was to apply the criteria for AKI based on the KDIGO classification in a population of patients with preoperative SCr above normal limits after cardiac surgery [coronary artery bypass grafting (CABG) or cardiac valve surgery (CVS)] and to evaluate acute worsening of renal function as a predictor of risk of 30-day mortality.

# METHODS

### **Patient selection**

This was a single-center study. We carried out a retrospective evaluation in patients from the Cardiac Surgery Intensive Care Unit at a Brazilian Medical School Center. Demographics, type of surgery, laboratory data and information of pre, peri and postoperative periods were obtained from a prospectively collected database of 2,878 patients who were older than 18

years and had undergone isolated CABG (1,786) or CVS (1,092) from January 2003 to June 2013. We excluded 51 patients with incomplete data, 23 dialysis patients and 1,886 patients with preoperative SCr within normal limits (Men – SCr  $\leq$  1.30 mg/dL / Women – SCr  $\leq$  1.00 mg/dL). After applying the exclusion criteria, 918 patients were analyzed [549 (60%) underwent CABG and 369 (40%) underwent CVS] (Figure 1).

This study was approved by the local Research Ethics (CAAE: 5974/2008). Because of its observational nature, informed consent was waived. This research fully adheres to Resolution 466/2012 of the National Health Council (CNS).

### **Serum Creatinine Measurement**

The Jaffe colorimetric method (ADVIATM 1650, Bayer, Germany) was used to measure SCr concentration. The reference value for adults is 0.6 to 1.3 mg/dL for men and 0.6 to 1.0 mg/dL for women.

### Stages of AKI based on KDIGO Classification[11]

**Stage 1:** Increase in  $SCr \ge 0.3 \text{ mg/dL}$  (in 48 hours) or 1.5 to 1.9 multiplied by baseline (in 7 days);

Stage 2: 2.0 to 2.9 multiplied by baseline SCr;

**Stage 3:** 3.0 or more multiplied by baseline; increase in  $SCr \ge 4.0 \text{ mg/dL}$ ; or beginning of renal replacement therapy regardless of a previous KDIGO stage.

### **Data Analysis**

The criteria for AKI were applied in 918 patients in the first seven postoperative days. Due to lack of data on urinary output, only SCr was used to determine the categories of AKI. According to the changes in SCr, the patients were classified as no AKI (KDIGO 0) and AKI stages 1, 2 or 3, based on the KDIGO criteria. Glomerular filtration rate (eGFR) was estimated by the Cockcroft-Gault<sup>[12]</sup> equation. The risk of postoperative death was assessed by EuroSCORE<sup>[13,14]</sup>, in the absence of a specific tool for our population.

### **Statistical Analysis**

Variables are presented as absolute numbers and percentages or median and interquartile ranges (25th and 75th percentile) when applicable. Continuous variables were compared using the nonparametric Mann-Whitney or Kruskal-Wallis tests, and the chi-square or Fisher's exact test was used to compare categorical variables.

Table 1. Classification and staging for RIFLE, AKIN, and KDIGO criteria.

	RIFLE		AKIN		KDIGO
Class	SCr or GFR	Stage	SCr	Stage	SCr
Risk	Increased Scr x 1.5 or GFR decrease > 25% (within 7 days)	1	Increase in SCr $\geq$ 0.3 mg/dL or $\geq$ 150% to 200% (1.5- to 2-fold) from baseline (within 48 hours)	1	Increase in SCr by $\geq 0.3$ mg/dL within 48 hours or increase in SCr 1.5 to 1.9 times baseline which is known or presumed to have occurred within the prior 7 days
Injury	Increased Scr x 2.0 or GFR decrease > 50%	2	Increase in SCr to more than 200% to 300% (> 2- to 3-fold) from baseline	2	Increase in SCr to 2.0 to 2.9 times baseline
Failure	Increased Scr x 3.0 or GFR decrease $> 75\%$ or SCr $\ge 4.0$ mg/dL or acute increase $\ge 0.5$ mg/dL	3	Increase in SCr to more than 300% (> 3-fold) from baseline or SCr ≥ 4.0 mg/dL with an acute increase of at least 0.5 mg/dL or initiation	3	Increase in SCr to 3.0 times baseline or increase in SCr to ≥ 4.0 mg/dL or initiation of renal replacement therapy
Loss	Persistent acute renal failure = complete loss of kidney function > 4 weeks		of renal replacement therapy		
End Stage Kidney Disease	End stage of kidney disease (> 3 months)				

Modified from Bellomo et al.<sup>[7]</sup>, Mehta et al.<sup>[8]</sup> and Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group<sup>[11]</sup>

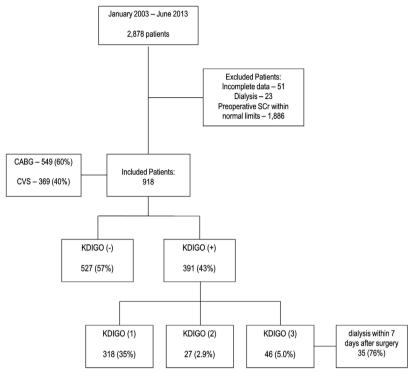


Fig. 1 - Study flow chart showing patients underwent cardiac surgery and staging for acute kidney injury (AKI) based on the KDIGO criteria.

CABG - coronary artery bypass grafting; CVS - cardiac valve surgery; PO - postoperative day

Univariate and multivariate Cox proportional hazards models (stepwise) were used to determine the association between AKI and 30-day mortality. The model was adjusted for age (years), gender (reference – female gender), type of surgery (reference – CVS), body mass index (kg/m²), diabetes mellitus (reference – non-diabetic), left ventricular function (reference – preserved left ventricular ejection fraction), cardiopulmonary bypass (CPB) times (min) and AKI (reference – KDIGO 0). The adjusted Hazard Ratio (HR) and 95% confidence intervals (95% CI) were calculated for the predictors. Cumulative survival graphics were built to demonstrate the AKI impact as a predictor of 30-day mortality. *P* values<0.05 were considered statistically significant (two-tailed). The data were analyzed using the IBM SPSS Statistical Package v.20 (IBM Corporation, Armonk, NY).

### **RESULTS**

Baseline characteristics of the patients are shown in Table 2. Median age was 61 years and 52% of the patients were male. Twenty-seven percent of the patients had preoperative eGFR above 60 mL/min. SCr measured in the immediate postoperative period was slightly lower than the preoperative SCr suggesting hemodilution during surgery (Table 3).

Of the 918 patients studied, 391 (43%) developed AKI: 318 (35%) stage 1, 27 (2.9%) stage 2 and 46 (5.0%) stage 3 (Table 3). Fewer patients in stage 2 may be because the indication for dialysis automatically classifies the patient in stage 3. Any degree of AKI was associated with a significant increase in overall mortality at 30 days compared with patients with no AKI (Table 4). In univariate analysis, the hazard ratio for death at 30 days was 5.4 for patients with KDIGO stage 1, 16.8 for patients with KDIGO stage 2 and 27.2 for patients with KDIGO stage 3 (*P*<0.001 for all).

Patients with AKI had higher EuroSCORE scores, but there was no difference in the percentage of patients at low, intermediate and high risk among the groups (Table 5). The 30-day mortality rate increased progressively in all KDIGO stages (Table 4). Time on CPB and intensive care length of stay also increased (Table 5). The proportion of patients who required mechanical ventilation for more than 24 hours after surgery increased from 6.3% for patients with KDIGO 0 to 67% among those with KDIGO 3 (Table 5). Of the patients with KDIGO 3, 76% required dialysis with a 30-day mortality rate of 66%. However, patients treated with dialysis were more severely ill, as demonstrated by the EuroSCORE calculated preoperatively [4 (2-6) vs. 8 (5-10)], *P*<0.001.

Table 2. Baseline characteristics of patients who underwent cardiac surgery.

	All Patients $(n = 918)$
	Median (Q1 – Q3) or N (%)
Type of surgery	
Coronary artery bypass grafting	549 (60)
Cardiac valve surgery	369 (40)
Multiple cardiac valve surgery	156 (42)
Cardiac valve surgery during active infective endocarditis	38 (10)
Age (years)	61 (52 - 68)
Male gender	477 (52)
Weight (kg)	70 (61 - 80)
Height (m)	1.63(1.56-1.70)
Body mass index (kg/m <sup>2</sup> )	26 (23 - 29)
Diabetes Mellitus	248 (27)
Left Ventricular Systolic Dysfunction (moderate/severe)	203 (22)
Intra-aortic balloon pump	43 (7.8)
Reoperation	134 (15)
Additive EuroScore	4 (2 - 6)
Low risk $(< 3)$	248 (27)
Intermediate risk (3 to 5)	402 (44)
High risk (5)	268 (29)
Cardiopulmonary bypass	781 (85)
Total cardiopulmonary bypass time (min)	94 (79 - 114)
< 90 min	312 (40)
90 - 120 min	308 (40)
> 120 min	161 (20)
Total number of grafts	3 (2 - 3)
Total Intensive Care length of stay	3 (2 - 6)

Q1= percentile 25; Q3= percentile 75; N= number of individuals

Table 3. Renal function of patients who underwent cardiac surgery.

	All Patients $(n = 918)$
	Median (Q1 – Q3) or N (%)
Preoperative SCr (mg/dL)	1.40 (1.20 – 1.60)
Preoperative eGFR (mL/min)	49 (39 - 60)
eGFR ≥ 90 mL/min	17 (20)
eGFR 60 – 89 mL/min	231 (25)
eGFR 30 – 59 mL/min	603 (66)
eGFR ≤ 29 mL/min	67 (70)
Serum creatinine (mg/dL)	
Immediate postoperative day	1.30 (1.10 - 1.60)
1 <sup>st</sup> Postoperative day	1.50 (1.20 - 1.90)
2 <sup>nd</sup> Postoperative day*	1.30 (1.0 - 1.80)
AKI in the first 7 days postoperatively	391 (43)
KDIGO Stage 0	527 (57)
KDIGO Stage 1	318 (35)
KDIGO Stage 2	27 (2.9)
KDIGO Stage 3	46 (5.0)
RRT in the first 7 days postoperatively	35 (3.8)

Q1 - percentile 25; Q3 - percentile 75; SCr - serum creatinine; eGFR - estimated glomerular filtration rate; RRT - renal replacement therapy.

<sup>\*</sup>There was no determination of SCr on 2<sup>nd</sup> postoperative day for 34 patients

Table 4. Postoperative complications of patients who underwent cardiac surgery.

	All Patients $(n = 918)$
	N (%)
Readmission to the intensive care unit from the ward	73 (8.0)
Prolonged intensive care length of stay (> 14 days)	97 (11)
Bleeding requiring surgical reintervention	27 (2.9)
New atrial fibrillation	86 (9.4)
Postoperative reintubation (within the first 7 days)	79 (8.6)
Mechanical ventilation > 24 hours	135 (17)
Mediastinitis	30 (3.3)
Type I neurological injury	42 (4.6)
30-day mortality	96 (10)
KDIGO Stage 0	15 (2.8)
KDIGO Stage 1	46 (14)
KDIGO Stage 2	10 (37)
KDIGO Stage 3	25 (54)

Q1 - percentile 25; Q3 - percentile 75; N - number of individuals

Table 5. Demographic data of patients who underwent cardiac surgery based on the KDIGO criteria.

	KDIGO 0	KDIGO 1	KDIGO 2	KDIGO 3	
	N = 527	N = 318	N = 27	N = 46	
	Median $(Q1 - Q3)$	<i>P</i> -value			
	or N (%)	or N (%)	or N (%)	or N (%)	
Coronary artery bypass grafting	319 (61)	190 (60)	16 (59)	24 (52)	0.745
Cardiac valve surgery	208 (39)	128 (40)	11 (41)	22 (48)	
Multiple CVS	81 (15)	60 (19)	5 (19)	10 (22)	0.533
CVS during active IE	21 (4.0)	9 (2.8)	1 (3.7)	7 (15)	0.006
Age (years)	60 (51 - 67)	63 (55 - 59)	64 (58 - 70)	66 (56 - 73)	< 0.001
Male gender	250 (47)	185 (58)	13 (48)	29 (63)	0.009
Weight (kg)	70 (61 - 79)	71 (62 - 80)	70 (65 - 82)	69 (57 - 83)	0.444
Height (m)	1.62(1.55 - 1.69)	1.64(1.57 - 1.70)	1.62(1.52 - 1.68)	1.66(1.60 - 1.72)	0.049
Body mass index (kg/m²)	26 (24 - 30)	27 (24 - 29)	28 (24 - 32)	25 (22 - 29)	0.150
Diabetes Mellitus	127 (24)	103 (32)	9 (33)	9 (20)	0.032
LVSD (moderate/severe)	118 (22)	71 (22)	6 (22)	8 (17)	0.890
Intra-aortic balloon pump	18 (3.4)	19 (6.0)	3 (11)	3 (6.5)	0.081
Preoperative SCr (mg/dL)	1.40 (1.20 - 1.60)	1.50 (1.30 - 1.80)	1.40 (1.20 - 1.40)	1.65 (1.40 - 2.10)	< 0.001
Preoperative eGFR (mL/min)	51 (42 - 63)	47 (38 - 58)	53 (45 - 65)	39 (28 - 52)	< 0.001
Reoperation	63 (12)	52 (16)	5 (19)	14 (30)	0.004
Additive EuroSCORE	4 (2 - 5)	4 (2 - 6)	5 (2 - 7)	7 (4 - 9)	< 0.001
Low risk (< 3)	187 (35)	115 (36)	8 (30)	22 (48)	
Intermediate risk (3 to 5)	218 (41)	126 (40)	8 (30)	18 (39)	0.190
High risk (5)	122 (23)	77 (24)	11 (41)	6 (13)	
CPB	422 (80)	293 (92)	25 (93)	41 (89)	< 0.001
Total CPB time (min)	90 (76 - 109)	100 (84 - 116)	100 (76 - 122)	110 (90 - 145)	< 0.001
< 90 min	190 (36)	106 (33)	12 (44)	16 (35)	
90 - 120 min	170 (32)	109 (34)	9 (33)	18 (39)	0.658
> 120 min	74 (14)	61 (19)	4 (15)	8 (17)	
Total ICU length of stay	2 (2 - 4)	3 (2 - 8)	4 (2 - 12)	8 (3 - 19)	< 0.001
Mechanical ventilation > 24 hours	33 (6.3)	60 (19)	11 (41)	31 (67)	< 0.001

CVS - cardiac valve surgery; IE - infective endocarditis; LVSD - left ventricular systolic dysfunction; SCr - serum creatinine; eGFR - estimated glomerular filtration rate; CPB - cardiopulmonary bypass; ICU - intensive care unit

Table 6. Cox proportional hazard model considering all patients who underwent cardiac surgery for predictors of 30-day mortality.

	HR (CI 95%)	P-value
Age (years)	1.03 (1.01 - 1.05)	0.007
Male gender	0.63 (0.42 - 0.95)	0.028
Total cardiopulmonary bypass time (min)	1.01(1.01 - 1.02)	< 0.001
KDIGO Stage 0	Reference	
KDIGO Stage 1	4.76(2.55 - 8.88)	< 0.001
KDIGO Stage 2	13.54 (5.77 – 31.78)	< 0.001
KDIGO Stage 3	20.81 (10.14 – 42.69)	< 0.001

HR - Hazard Ratio; CI - confidence interval

### Cox regression analysis

In a multivariate analysis, age (years), CPB time (minutes) and AKI (KDIGO 1-3) were independent predictors of 30-day mortality, with KDIGO stage 3 being the strongest predictor. Male gender had a reduced risk of death at 30 days (Table 6, Figure 2). Subgroup analysis (CABG and CVS) demonstrated similar results, except for reduced risk of death among male patients who underwent CABG (data not shown).

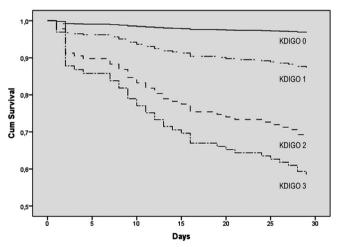


Fig. 2 - Overall survival curves of patients who underwent cardiac surgery, according to the KDIGO criteria.

## DISCUSSION

In our study, AKI after CABG or CVS was found to be common and associated with high rates of prolonged intensive care length of stay, morbidity and mortality. This study also demonstrated the importance of KDIGO AKI criteria as a powerful predictor of 30-day mortality in patients with preoperative SCr above normal limits. We found a higher risk of death in those with poor renal function as well as those who required dialysis; however, even slight increases in SCr postoperatively (KDIGO stage 1) were associated with a significant increase in mortality.

The reasons why small changes in SCr correlated with increased hospital mortality are not entirely clear. Possible explanations include the adverse effects of decreased renal function, such as volume overload, anemia, uremia, acidosis, electrolyte disturbances, and increased risk of infections<sup>[11,15]</sup>. Visual analysis of the survival curves graph of our study showed a continuous decrease of survival in patients who developed AKI, with a higher risk of death within the first week postoperatively (Figure 2).

Preoperative renal dysfunction is known as a postoperative risk predictor; however, in tools such as EuroSCORE<sup>[13,14]</sup>, InsCor<sup>[16]</sup>, and Parsonnet<sup>[17]</sup>, preoperative renal dysfunction is considered a risk factor only in cases of advanced kidney disease (SCr>2.00 or 2.26 mg/dL) or in patients on dialysis. In its update published in 2012, called EuroSCORE II<sup>[3]</sup>, assessment of renal function was included by calculating the eGFR, with values below 85 mL/min being a risk factor.

Estimates of preoperative renal function based on eGFR show that over 75% of patients undergoing CABG have an eGFR below 90 mL/min<sup>[18]</sup>, highlighting the importance and high prevalence of renal dysfunction in patients undergoing heart surgery. Furthermore, these patients are older and have more comorbidities, such as cerebrovascular disease, peripheral artery disease, chronic obstructive pulmonary disease and diabetes mellitus<sup>[18]</sup>.

Several studies have shown that slight changes in renal function have a significant impact on short and long term outcomes in patients undergoing cardiac surgery<sup>[5,19-23]</sup>. Other studies suggest that intraoperative factors such as CPB times are important contributors to postoperative renal dysfunction<sup>[24-26]</sup>, as observed in our study (OR 1.01 - 95% CI 1.01 to 1.02, P value<0.001 - data not shown), but others have not demonstrated this direct relationship<sup>[27,28]</sup>. The use of off-pump CABG was also tested in preoperative renal dysfunction with contradictory results<sup>[18,29,30]</sup>.

Many publications have reported preoperative renal dysfunction as a risk predictor for morbidity and postoperative mortality. Kumar et al. [31] identified class III obesity (BMI >  $40~kg/m^2$ ) as an independent predictor of AKI after on-pump CABG, and Brown et al. [32] found high rates of readmission within 30 days after cardiac surgery in patients who developed

AKI. Zakeri et al.<sup>[22]</sup> evaluated patients with mild to moderate impaired renal function (SCr < 2.26 mg/dL) who underwent CABG. Operative mortality was higher in this group of patients as well as the need for dialysis and occurrence of stroke postoperatively. Both the measurement of SCr as well as eGFR (< 60 mL/min) were independent predictors of hospital mortality and in a 3-year follow-up. Cooper et al.<sup>[33]</sup> evaluated more than 483,000 patients using the American Society of Thoracic Surgeons database. Seventy-eight percent of patients had some degree of preoperative (CrCl < 90 mL/min) renal dysfunction. Mortality was inversely proportional to the renal function. In an adjusted model, the eGFR was one of the strongest predictors of morbidity and hospital mortality.

# **Study limitations**

Our study has several limitations. First, these data originated from a single center. Although data were collected prospectively, the analysis was performed retrospectively. There was no determination of cause of death, which did not allow us to differentiate between cardiovascular death and death from all causes. Several known and unknown confounding variables could theoretically have influenced the observed mortality rates. Despite the use of multivariate models for control and adjustment of some of these variables, the possibility of the presence of other unknown confounders cannot be ruled out.

### CONCLUSION

The development of AKI, based on KDIGO criteria, correlated with increased morbidity and was a robust predictor of 30-day mortality in patients with preoperative baseline SCr above normal limits undergoing coronary artery bypass grafting or cardiac valve surgery.

Authors' roles & responsibilities		
MNM	Design of the project; data collection; statistical analysis; discussion of results; manuscript writing	
MAN	Discussion of results; manuscript writing, article review	
LNM	Discussion of results; manuscript writing, article review	

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