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Risk factors for acute kidney injury after cardiac surgery

Fatores de risco para lesão renal aguda após cirurgia cardíaca

Alfredo José RODRIGUES[1], Paulo Roberto Barbosa EVORA[2], Solange BASSETTO[3], Lafaiete ALVES JÚNIOR[3], Adilson SCORZONI FILHO[3], Wesley Ferreira ARAÚJO[3], Walter Vilella Andrade VICENTE[4]

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Abstract

Objective: **The objective of the present investigation was to identify risk factors for acute kidney injury in patients with normal levels of serum creatinine who underwent coronary artery bypass graft (CABG) surgery and/or valve surgery.**

Methods: **Data from a cohort of 769 patients, after the exclusion criteria were applied, were analyzed using bivariate analyses and binary logistic regression modeling.**

Results: **Three hundred eighty one patients experienced CABG, 339 valve surgery and 49 went through both simultaneously. Forty six percent of the patients were female and the mean age was 57±14 years (13 to 89 years). Seventy eight patients presented renal dysfunction postoperatively (10%), of these 23% needed hemodialysis (2.4% of all patients). The mortality for the whole cohort was 10%. The overall mortality for patients experiencing postoperative renal dysfunction was 40 % (versus 7%, *P*<0.001), 29% for those who did not need dialysis and 67% for those who needed dialysis (*P*=0.004). The risk factors that were independently associated with AKI were: age (*P*<0.000, OR: 1.056), congestive heart failure (*P*=0.091, OR: 2.238), COPD (*P*=0.003, OR: 4.111), Endocarditis (*P*= 0.001, OR: 12.140, myocardial infarction < 30 days (p=0.015, OR: 4.205), valve surgery (*P*=0.016, OR: 2.137), cardiopulmonary bypass time >120 min (*P*=0.001, OR: 7.040), peripheral arterial vascular disease (*P*=0.107, 2.296).**

Conclusion: **Renal dysfunction was the most frequent postoperative organ dysfunction in patients who underwent CABG and/or valve surgery and age, congestive heart failure, COPD, Endocarditis, myocardial infarction < 30 days, valve surgery, cardiopulmonary bypass time >120 min, and peripheral arterial vascular disease were the risk factors independently associated with AKI.**

Descriptors: **Kidney Failure, Acute. Cardiac Surgical Procedures. Risk Factors. Risk Management.**

Resumo

Objetivo: **Identificar fatores de risco associados à lesão renal aguda em pacientes com níveis séricos normais de creatinina sérica que foram submetidos à revascularização cirúrgica do miocárdio e/ou cirurgia valvar.**

Métodos: **Os dados de uma coorte de 769 pacientes foram analisados utilizando análise bivariável e regressão logística binária.**

Resultados: **Trezentos e oitenta e um pacientes foram submetidos à revascularização isolada, 339 a cirurgia valvar**

1. Post-Doctorate (Professor of the Cardiovascular and Thoracic Surgery Division at Ribeirão Preto Medical School – USP)
3. Master's Degree (Assistant Physician of the Cardiovascular and Thoracic Surgery Division at Ribeirão Preto Medical School – USP)
4. Master's Degree (Assistant Physician of the Cardiovascular and Thoracic Surgery Division at Ribeirão Preto Medical School – USP)
5. Full Professor (Head of the Cardiovascular and Thoracic Surgery Division at Ribeirão Preto Medical School – USP)

This study was carried out at the Cardiovascular and Thoracic Surgery Division at Ribeirão Preto Medical School – University of São Paulo – Ribeirão Preto, SP, Brazil.

Correspondence address:
Alfredo J Rodrigues. Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, Departamento de Cirurgia e Anatomia. Av. Bandeirantes, 3.900 - Campus Universitário-Monte Alegre, Ribeirão Preto, SP, Brasil. CEP: 14048-900.
E-mail: alfredo@fmrp.usp.br

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e 49 a ambas. Quarenta e seis por cento dos pacientes eram do sexo feminino e a idade média foi 57 ± 14 anos. Setenta e oito (10%) pacientes apresentavam disfunção renal no pós-operatório, 23% destes necessitaram hemodiálise. A mortalidade geral foi 10%. A mortalidade para pacientes com disfunção renal pós-operatória foi de 40% (*versus* 7%, *P* <0,001), 29% para aqueles que não precisam diálise e 67% para aqueles que necessitaram de diálise (*P* = 0,004). Os fatores de risco independentes identificados foram: idade (*P* <0,000, OR: 1,056), insuficiência cardíaca congestiva (*P* = 0,091, OR: 2,238), DPOC (*P* = 0,003, OR: 4,111), endocardite (*P* = 0,001, OR: 12,140, infarto do miocárdio < 30 dias (*P* = 0,015, OR: 4,205), cirurgia valvar (*P* = 0,016, OR: 2,137), tempo de circulação extracorpórea > 120 minutos (*P* = 0,001, OR: 7,040), doença arterial periférica (*P* = 0,107, 2,296).

***Conclusão:* A disfunção renal foi a disfunção orgânica pós-operatória mais frequente em pacientes submetidos à revascularização do miocárdio e/ou cirurgia valvar e idade, presença de insuficiência cardíaca, DPOC, endocardite, infarto do miocárdio < 30 dias, doença arterial periférica, cirurgia valvar e tempo de circulação extracorpórea > 120 minutos foram os fatores de risco independentemente associados à lesão renal aguda.**

***Descritores:* Procedimentos cirúrgicos cardiovasculares. Falência renal aguda. Fatores de Risco.**

INTRODUCTION

Acute kidney injury (AKI) is a prevalent and prognostically important complication of cardiac surgery [1]. When the injury is severe enough to necessitate dialysis, it may confer a pronounced increase in the odds of death [2], and even less severe injury may be associated with markedly increased morbidity and mortality [3]. The ability of preoperatively identify patients at risk for AKI may present the opportunity for making use of preventive strategies to mitigate the risk [4]. Therefore, the aim of the present investigation is to identify perioperative risk factors for perioperative AKI resulting in postoperative renal dysfunction in patients without clinical evidence of preoperative renal dysfunction who had undergone valve heart surgery and/or coronary artery bypass graft surgery (CABG).

METHODS

Data from a prospectively collected database were used for the present study. The initial cohort consisted of 924 patients > 12 year, independently of race or gender, who had undergone valve heart surgery and/or CABG with cardiopulmonary bypass (CPB) at the Clinics Hospital at Ribeirão Preto Medical School of University of São Paulo between January 2003 and July 2009. Exclusion criteria for the present study were preoperative serum creatinine > 1.5 mg/dl or < 0.7 mg/dl, preoperative dialysis, preoperative known renal disease, preoperative urinary infection, any cardiac operation performed without cardiopulmonary bypass, any other cardiac procedure besides heart valve surgery and/or CABG surgery. For patients who underwent more than 1 relevant procedure during the study period, only data on their initial surgery were collected. All the patients had their serum creatinine assessed within 30 days before surgery. If there is more than one assessment within 30 days, the most recent was used independently of its value. In our hospital the normal range for serum creatinine is between 0.7 and 1.5 mg/dl.

Postoperative acute kidney injury was defined as an increase of at least 50% in preoperative serum creatinine value independently if postoperative dialysis was or was not needed. After research board approval of our hospital was received, detailed perioperative data were analyzed retrospectively.

Dependent and independent variables

The primary dependent variable was postoperative AKI, as defined above. Measurements of preoperative and intraoperative variables known to be or that could potentially be associated with AKI (independent variables) were examined. Patients with systolic pulmonary artery pressure > 40 mmHg were classified as having hypertension and patients with myocardial infarction were divided into infarction patients with less or more than 30 days. Any patient with a previous diagnosis of diabetes mellitus in nutritional or medical treatment or any patient with fasting glucose above 110 mg/dl was considered as suffering diabetes mellitus. It was considered as a victim of stroke, any patient with a definite diagnosis by neurological evaluation, regardless of whether or not neurological sequelae. The definition of the other independent variables was defined according the EuroSCORE [5].

Statistical analysis

Categorical variables were summarized as frequencies and percentages and continuous variables as means and standard deviations. To compare more than 2 groups ANOVA plus Games-Howell post hoc test was used. The unadjusted association of the preoperative and intraoperative variables with AKI rates was calculated (with the Mann-Whitnney test and the X^2 statistic). Binary logistic regression modeling was also performed to assess the adjusted associations of measured perioperative variables with the postoperative AKI. Initially, bivariate analyses (using the X^2 statistic for categorical variables and Mann-Whitney test for continuous variables) were performed to identify which variables were associated with the dependent variables. The linearity relationship between the continuous predictor variables and AKI was assessed with Box-Tidwell transformation [6]. Variables that were not linearly related were categorized along clinically sensible cut points. All clinically sensible variables with $P<0.3$ in the bivariate analyses were entered into logistic regression models. Subsequent retention in the models was determined by backward stepwise selection, in which $P<0.15$ was the criterion for variable retention. Collinearity statistics (tolerance and variance-inflation factor) was performed to identify collinear independent variables. Model discrimination and calibration were assessed by the c-index and the Hosmer-Lemeshow statistic (larger probability value means better calibration), respectively. SPSS version 16.0 (SPSS, Inc, Chicago, IL, USA) was used for the statistical analyses.

RESULTS

After the exclusion criteria were applied, 769 patients were included in the study. Three hundred eighty one patients underwent CABG, 339 underwent valve surgery and 49 underwent both simultaneously. Demographic and operative data are shown in Table 1. Forty three percent of the patients who underwent valve operation needed mitral replacement, 13% mitral valve repair, 30% aortic valve replacement and 7% had mitral and aortic valve replacement. Among those who underwent CABG surgery the number of distal anastomosis was 2.9±0.9. Patients who underwent isolated valve operation were younger (51±15 years versus 62±10 years, $P<0.001$), had worst functional class (52% was in Class III/IV versus 8%, $P<0,001$) and needed longer CPB time (113±50 min. versus 97±52 min., $P<0.001$) than those who underwent isolated CABG. The CPB time was even longer in patients needing combined operation compared with isolated CABG or valve surgery (153±62 min, ANOVA plus Games-Howell post hoc test).

Seventy eight patients (10%) presented renal dysfunction postoperatively, of these 23% needed hemodialysis (2.4% of all patients). The overall hospital mortality was 10%. The mortality for patients experiencing postoperative AKI was 40 % (versus 7%, $P<0.001$). The mortality was 29% for those experiencing AKI postoperatively who did not need dialysis, and 67% for those who needed dialysis ($P=0.004$). The hospital course of the patients is presented in Table 2.

Table 1. Demographics

	N	%
Female	356	46.3%
Age	57 ± 14 (13-89 years)	
BMI	26.0 ± 4.6	
Functional Class NYHA		
I	303	40.2%
II	222	29.5%
III	198	26.3%
IV	30	4.0%
Ejection Fraction	0.56 ± 0.13	
Chronicle Atrial Fibrillation	126	16.4%
Diabetes mellitus	212	27.6%
Carotid disease	19	2.5%
Preop. critical status	18	2.4%
COPD	33	4.3%
Previous Stroke	42	5.5%
Peripheral arterial dis.	43	5.6%
Endocarditis	11	1.4%
Arterial hypertension	473	61.5%
Smoke	132	17.2%
Myocardial Infarction < 30days	28	3.6%
Myocardial Infarction >30 days	191	24.8%
PASP > 40 mmHg	94	12.2%
Aortic clamp time (min)	77 ± 38	
CPB time (min)	108 ± 54	
Non-elective op	57	7.4%
Previous Cardiac op	123	16.0%

BMI = Body Mass Index; PASP = pulmonary artery systolic pressure; COPD =Chronic Obstructive Pulmonary Disease; CPB = Cardiopulmonary bypass; NYHA =New York Heart Association

Table 2. Hospital course

	N	%
Acute Renal injury	78	10%
Dialysis	18	2.4%
Reoperation for bleeding	39	5%
Mechanical ventilation> 48h	81	10%
Pneumonia	30	4%
Wound infection	23	3%
Cardiac dysfunction	46	6%
Stroke	25	3%
Acute Myocardial infarction	40	5%
Mortality	81	10%

The bivariate associations of patient-related variables with postoperative AKI are shown in Table 3. The following variables entered into the initial logistic regression model: age, CPB times, NYHA Class III or IV, chronic atrial fibrillation, diabetes mellitus, carotid disease, critical preoperative state, COPD, peripheral vascular disease, endocarditis, myocardial infarction <30 days, valve operation, myocardial revascularization, valve operation and revascularization myocardium, previous cardiac operation, systolic pulmonary pressure ≥ 50 mmHg, non-elective operation, congestive heart failure. The results of the binary logistic regression are presented in Table 4.

Table 3. The bivariate associations of patient-related variables with postoperative AKI

Variable	Without Postop-AKI	With Postop-AKI	Odds ratio	*P*
Age (Y)	56±13	64±11	-	>0.001
Class III/IV NYHA	29%	43%	1.8	0.013
Class IV NYHA	3,5%	8%	2.4	0.069
Chronicle AF	16%	23%	1.6	0.069
Diabetes	27%	35%	1.4	0.142
Carotid disease	2%	5%	2.4	0.111
Preop. critical status	2%	8%	5.0	0.001
COPD	3%	13%	4.3	<0.001
Peripheral arterial dis.	5%	11%	2.5	0.016
Endocarditis	1%	8%	7.8	<0.001
CHF	4%	14%	3.7	<0.001
MI <30 days	3%	9%	3.1	0.008
Non-elective op.	6%	15%	2.6	0.005
CPB time (min)	105±53	132±54	-	<0.001
CABG	50%	42%	0.723	0.177

CHF, congestive heart failure; Preop. critical status, preoperative critical status; COPD chronic obstructive pulmonary disease; MI myocardial infarction; CPB cardiopulmonary bypass; Peripheral arterial dis., peripheral arterial vascular disease; NYHA =New York Heart Association; CABG = coronary artery bypass graft surgery

The model demonstrated good discrimination (area = 0.792, 95% CI: 0.738-0.847, *P*<0.001) and calibration (Hosmer-Lemeshow statistic: 0.304).

DISCUSSION

In the present study renal dysfunction was the most frequent organ dysfunction occurring postoperatively, since the need for prolonged mechanical ventilation, equally frequent, was also related to others organic dysfunction besides lung injury. We have identified several preoperative risk factors for AKI, most of them directly or indirectly related to poor hemodynamic status and/or arterial disease, such as peripheral arterial disease, carotid artery disease and myocardial infarction, similarly to other investigators [7-12]. However, in our cohort, CABG surgery alone was not an independent factor associated with postoperative AKI, contrarily to valve surgery, even though coronary artery disease is intimately associated with older age, diabetes mellitus, COPD and peripheral atherosclerosis. The finding that valve operation is a risk factor for AKI is not surprising, and it may be explained due the fact of valve dysfunction, in spite of affecting younger patients in our country, requires a more complex intracardiac operation, usually involving mitral reconstruction or replacement. In addition, usually valve operations demand longer CPB times, an independent risk factor for AKI, and frequently are performed in patients with hemodynamic status more compromised than those with isolated coronary disease, as we have demonstrated.

Others have found results similar to ours. Palomba et al. [13] developed an acute kidney injury score analyzing preoperative, intraoperative and early postoperative variables of a cohort of 603 patients who underwent elective CABG, valve surgery, or both. Combined surgery, functional class of NYH >2, preoperative serum creatinine > 2 mg/dl,

Table 4. Results of the binary logistic regression

	Coefficient	S.E.	Wald	Sig	Odds ratio	95% C.I. for Odds ratio	
						Lower	Upper
Age	0.054	0.013	18.802	0.000	1.056	1.030	1.082
CHF	0.806	0.476	2.865	0.091	2.238	0.881	5.689
COPD	1.414	0.471	8.995	0.003	4.111	1.632	10.355
Endocarditis	2.497	0.753	11.002	0.001	12.140	2.777	53.076
MI < 30 days	1.436	0.590	5.921	0.015	4.205	1.322	13.374
Valve surgery	0.759	0.316	5.786	0.016	2.137	1.151	3.968
CPB>120 min	1.952	0.562	12.047	0.001	7.040	2.339	21.195
Peripheral arterial dis.	0.831	0.515	2.605	0.107	2.296	0.837	6.300
Constant	-7.332	0.994	54.420	0.000	0.001		

CHF, congestive heart failure; COPD chronic obstructive pulmonary disease; MI myocardial infarction; CPB cardiopulmonary bypass; Per. art. vasc. dis peripheral arterial vascular disease

low cardiac output, age>65 years old, cardiopulmonary bypass time> 120 min, preoperative capillary glucose>140 mg/dl and central venous pressure > 14 cm H_2O were the selected variables. Grayson et al. [14] analyzing 5,132 consecutive patients who underwent cardiac operation using cardiopulmonary bypass, also excluding patients with significant preoperative renal impairment, found that valve surgery was an independent risk factor for the development of postoperative acute renal dysfunction. Chertow et al. [7], in a study involving 42,773 patients who had undergone cardiac operations, also showed that valve operation was an independent predictor for AKI. Kochi et al. [10], although in a smaller sample, also found that age, ventricular dysfunction, myocardial infarction and peripheral vascular disease were independently associated with postoperative renal dysfunction.

Among several causes of AKI after cardiac surgery one of the most important is cellular ischemia [15], since blood pressure during cardiac surgery is often at the lower limits or even below the limits of autoregulation of the blood flow. In addition, many cardiac surgery patients may have impaired autoregulation of kidney blood flow due perioperative administration of medications. Also, systemic inflammation provoked by the cardiopulmonary bypass plays a preponderant role in the development of kidney injury by promoting proinflammatory events that amplify the operative trauma [16], and certainly microemboli during cardiopulmonary bypass is also an important factor.

In the present study the number of patients who underwent CABG surgery in combination with valve surgery represented less than 7% of the cohort, compromising its collaboration in the developed model. However, our intention was not to develop a model for precise prediction of AKI, since we believe our sample size was not ideal for this purpose. Our main concern was to find preoperative variables that may be associated with AKI and identify those suitable for prophylactic intervention. However, in spite of the efforts, it seems there is a the lack of progress in preventing AKI and its consequences after cardiac surgery [4] that may be related to the difficulties with the proper definition of AKI and the initiation and timing of dialysis [17, 18]. Nonetheless, some preoperative and intraoperative preventive actions may help to prevent the postoperative renal dysfunction. Postponing the operation to improve the hemodynamic situation [19], stopping medications, such as angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, shortly before the operation [20], planning the surgical strategy to shorten the cardiopulmonary bypass time, and a tight perioperative glucose control [21] may help to reduce the incidence of postoperative renal dysfunction. N-acetylcysteine, B-type natriuretic peptide and other drugs have been proposed to reduce postoperative AKI or improve the renal function, however their use has been controversial [4]. Although it is obvious that intraoperative and postoperative adverse events may contribute to the occurrence of postoperative renal dysfunction, many of them are not predictable, and therefore their use for preoperative risk stratification of AKI may be limited.

There are limitations to this study. We believe that our sample size was not large enough to develop a highly accurate model to stratify renal risk, and ideally our results should be validated using an external sample. Other important preoperative variables, such as medications in use and the condition of other organic functions - like the hepatic, hematopoietic and haemostatic functions - should be of concern, mainly in patients who have already presented preoperative renal dysfunction and/or has been enduring congestive heart failure for long time. In addition, the variables associated with postoperative AKI, as well as their value, may be different according to the preoperative baseline renal function [9,22]. However, the cost-effectiveness and practicality of a more accurate preoperative evaluation of the renal and other organic function must be considered before becoming routinely used.

CONCLUSION

In conclusion, renal dysfunction was the most frequent postoperative organ dysfunction in patients who underwent CABG and/or valve surgery and age, congestive heart failure, COPD, endocarditis, myocardial infarction < 30 days, valve surgery, cardiopulmonary bypass time >120 min, and peripheral arterial vascular disease were the risk factors independently associated with AKI.

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