Prevalence and risk factors for acute renal failure in the postoperative of coronary artery bypass grafting

Prevalência e fatores de risco para insuficiência renal aguda no pós-operatório de revascularização do miocárdio

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Abstract

Objective: To determine the prevalence, risk factors, and the clinical outcome of patients undergone coronary artery bypass grafting who progressed with Acute Renal Failure (ARF).

Methods: A prospective study was performed from data of 186 patients undergone surgery from January 2003 through June 2006. The stored data were analyzed using the software STATA 9.0.

Results: The prevalence of ARF was of 30.6% (57/186). In 7.0% (4/57) dialysis therapy was needed. The mean age of patients with and without ARF progression was 62.8 % (±9.4) years and 61.3% (±8.8) years respectively (*P*=NS). CPB time >115 min (p= 0.011) and cross-clamp time >85 min (p=0.044) were related to ARF by the univariate analysis. The need for intra-aortic balloon (*P*= 0.049), mechanical ventilation >24h (*P* = 0.006), Intensive Care Unit (ICU) stay > three days (*P*< 0.0001), bradycardia (*P*= 0.002), hypotension (*P*= 0.045), arrhythmia (*P*=0.005) and inotropic infusion (*P*= 0.0001) were higher in the ARF group. Only the ICU stay longer > 3 days showed statistical correlation with ARF by the multivariate analysis (*P*=0.018). The mortality rate with and without ARF was 8.8% (five cases) and 0.8% (one case) respectively (*P*=0.016), but it reached 50% (2/4) in dialytic patients.

Conclusion: ARF was a frequent and severe postoperative complication associated with higher mortality and longer ICU stay, which presented as risk factors: longer CPB and cross-clamp times, mechanical ventilation > 24h and hemodynamic instability.

Descriptors: Myocardial revascularization. Risk factors. Renal insufficiency, acute.

Resumo

Objetivo: Determinar a prevalência, fatores predisponentes e o desfecho clínico dos pacientes submetidos a cirurgia de revascularização do miocárdio que apresentaram insuficiência renal aguda (IRA).

Métodos: Estudo do tipo coorte prospectivo, a partir dos prontuários de 186 indivíduos submetidos a cirurgia, no período de janeiro de 2003 a junho de 2006. As informações foram inseridas em um banco de dados e analisadas pelo *software* STATA 9.0.

Resultados: A prevalência de IRA foi 30,6% (57/186), sendo que 7% (4/57) necessitaram de diálise. A idade média dos

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pacientes que evoluíram com IRA e sem IRA foi 62,8 ± 9,4 anos e de 61,3 ± 8,8 anos, respectivamente (*P*=NS). Na análise univariada, estiveram relacionados com IRA: tempo de CEC > 115 min (*P*=0,011) e tempo de pinçamento da aorta > 85 min (*P*=0,044). No pós-operatório, a necessidade de balão intra-aórtico (*P*=0,049), tempo de ventilação mecânica > 24h (*P*=0,006), permanência da UTI > três dias (*P*<0,0001), bradicardia (*P*=0,002), hipotensão (*P*=0,045), arritmia (*P*=0,005) e uso de inotrópicos (*P*= 0,0001) foram superiores no grupo com IRA. Na análise multivariada, apenas tempo de internação na UTI > três dias apresentou correlação com IRA (*P* = 0,018). A taxa de mortalidade nos pacientes com e sem IRA foi 8,8% (cinco casos) e 0,8% (um caso), respectivamente (*P*=0,016), atingindo 50% (2/4) entre os que necessitaram de diálise.

Conclusão: A IRA foi uma complicação pós-operatória frequente e grave associada à maior mortalidade e permanência na UTI, cujos fatores de risco observados foram: tempo prolongado de CEC e anoxia, ventilação mecânica > 24h e instabilidade hemodinâmica.

Descritores: Revascularização miocárdica. Fatores de risco. Insuficiência renal aguda.

INTRODUCTION

Acute renal failure (ARF) is one of the most serious and frequent complications observed in the postoperative period of heart surgery, with prevalence ranging from 1% in patients without prior renal disorder, and 16% to 20% among those with a history of some renal dysfunction [1]. The need for dialysis is observed in up to 30.6% of cases [2,3].

Multifactorial events (pre-, intra- and postoperative) may determine the onset of ARF after heart surgery, even in case of no cardiovascular dysfunction or nephrotoxicity in these patients [4]. In our country, Palomba et al. [5] found that the sum of preoperative factors (age > 65 years, creatinine > 1.2 mg/dL, capillary blood glucose > 140mg/dL, heart failure of functional class > II and combined surgery), intraoperative (duration of CPB > 120 minutes) and postoperative (low cardiac output, central venous pressure > 14cmH$_2$O) may promote the occurrence of ARF.

In patients undergoing heart surgery, it is noted a common volume depletion (because of bleeding during and after surgery) and loss of liquid for the third space (resulting from systemic inflammatory response), which compromises renal perfusion reducing the glomerular filtration rate (GFR) [4]. In the study by De Moraes Lobo et al. [6] it was observed that patients with reduced glomerular filtration rate (GFR) in the postoperative, require a greater infusion of volume and use of sodium nitroprusside and presented lower fractional excretion of sodium (FENa$^+$), suggesting that changes in renal function observed resulted from an appropriate renal response to low effective blood volume.

The presence of renal failure is an important risk factor for the increase in the number of deaths in the postoperative period of heart surgery [7]. Evidence suggests that small increases in serum creatinine in the postoperative period are associated with significant effects on the risk of death [8]. In general, it seems that mortality among patients undergoing heart surgery may reach 8% of cases, however, when presentation of ARF is established in the postoperative period of these patients, there is an exponential increase in risk of death, surpassing 60% of the cases [9].

Thus, it is necessary to perform the identification of factors associated with increased risk of progression to ARF in the postoperative period, so that preventive measures are taken, reducing the prevalence of the event, through the establishment of clinical (pre- and postoperative) and therapeutic approaches more effective, contributing to reduce morbidity and mortality among patients. This study aimed to determine the prevalence and predisposing factors for acute renal failure among patients undergoing coronary artery bypass grafting.

METHODS

Type of study

We performed a prospective study with data collected retrospectively from the medical records of 186 patients who had undergone a retrospective cohort surgery from data collected from medical records of patients who had undergone CABG surgery in our institution.

Sample

From January 2003 to June 2006, 406 patients underwent CABG surgery, and 186 of them were included in the study. The criteria for non-inclusion of the remaining patients were: 1 - age under 40 years; 2 - coronary artery bypass grafting without use of cardiopulmonary bypass, 3 - death within 24 hours after surgery, 4 - records without information on the creatinine value preoperatively (except in cases of patients who underwent dialysis in the postoperative period) or cardiopulmonary bypass time, and 5 - patients with Glomerular Filtration Rate (GFR) < 15 mL/min.

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Data collection

From the list of patients who had undergone surgery, records from patients who met the criteria for inclusion in the study were collected. Subsequently, we collected information on the identification data, laboratory tests, clinical presentation, monitoring and treatment applied.

The data were related to the preoperative period and ICU postoperative follow-up, characterized in six times, namely:

• *T0*: corresponded to the preoperative period, before induction of anesthesia;

• *T1*: from the admission of the patient to the ICU up to 6h59min of the next morning;

• T2: starting at 7am on the 1st postoperative day up to 6h59min of the next day or time of patient's death (if it had occurred 24 hours after the end of the procedure);

• T3: starting at 7am on the 2nd postoperative day up to 6h59min of the next day or time of discharge from ICU or patient's death;

• T4: starting at 7 am on the 3rd postoperative day up to 6h59min of the next day or time of discharge from ICU or patient's death;

• Discharge from ICU

Variables

We approached the following variables in this study:

Clinical data

• Age: in years, presented as mean ± standard deviation (SD) and age;

• Gender: male and female;

• Weight: in kg to calculate estimated Glomerular Filtration Rate (GFR) and daily diuresis;

• Personal comorbidities, as described in the medical records: diabetes mellitus, systemic arterial hypertension, GFR between 15-59 mL/min, previous heart surgery, acute myocardial infarction or angina pectoris, stroke, among others.;

• Underlying pathologies.

Complementary exams

• Serum creatinine (Cr_s): assessing prior renal function and daily postoperative follow-up up to discharge from the ICU. Reference value: 0.5 to 1.3 mg/dL.

• Urea: preoperative values and daily postoperative follow-up up to T4. Reference value: 30 to 40 mg/dL.

• Creatinine clearance (CrCl) was estimated by the Cockcroft-Gault method [10] to classify preoperative renal function, considering patients with moderate or severe renal failure those with GFR between 15-59mL/min [11].

Surgical data

• Number of surgical procedures performed, length of cardiopulmonary bypass (CPB), length of aortic clamping (AC) and total of anastomoses.

Data of postoperative monitoring

• Mean Arterial Pressure: obtained through the arithmetic mean of the highest and lowest blood pressure measurements recorded each day.

• Diuresis: presented in the form of mL/kg/day, by defining oliguria when the value is less than 1 mL/kg/day.

• Duration of mechanical ventilation: above 24 hours;

• Need for use of intra-aortic balloon (IAB);

• Length of stay in ICU;

• Complications: bleeding, hypotension (MAP < 65 mmHg), bradycardia (HR < 60 bpm), reoperation, cardiac arrhythmia and stroke (CVA);

• The need for dialysis;

• Use of inotropic drugs: dopamine and dobutamine, from the 2nd postoperative day (corresponding to T3);

• Occurrence of death.

Criteria for definition of ARF

We considered patients with acute renal failure postoperatively, those patients who presented [4]:

1) 50% increase in creatinine in the postoperative period, with baseline > 1.3 mg/dL preoperatively;

2) increase of 0.5 mg/dL in creatinine among those with preoperative value d" 1.3 mg/dL, or

3) need for dialysis postoperatively.

To calculate the prevalence of dialytic ARF, only patients who had undergone dialysis during the ICU stay were considered, excluding those who required dialysis after discharge from this unit.

Ethical aspects

The study was approved by the Research Ethics Committee of the Institution (Protocol No. 33104-0372/2007) as the Resolution 196/96 of the National Health Council for research involving humans.

Statistical analysis

First, descriptive analysis of the variables studied was performed. Qualitative variables are presented by frequencies and percentages, and quantitative variables as mean and standard deviation.

For comparison of quantitative variables we used the bilateral student's t test for independent samples and for the qualitative variables we used the Chi-square, where applicable, and Fisher's exact test. Normality of quantitative variables was analyzed by Shapiro Wilk test.

To identify factors associated with acute renal failure postoperatively, we performed univariate analysis using the model of logistic regression.

To establish the overall association of the factors

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studied with ARF, we used the model of logistic regression. Variables with a p-value less than 0.20, in the univariate analysis, were considered in the model of logistic regression analysis. The selection of variables was performed using the stepwise method by elimination. Only variables with p-value less than 0.05 remained in the final model. We also estimated the odds ratios (OR) and their respective confidence intervals of 95%. The data were analyzed using 9.0 STATA statistical software.

RESULTS

The mean age of patients was 61.7 ($\pm$ 8.9) years, and 61.8% were aged less than 60 years. Most of them were males (109 - 58.6%).

The prevalence of ARF in the postoperative period was 30.6% (57/186), and only 7.0% (4/57) required dialysis.

Of the total patients, 27 (15.1%) presented preoperative serum creatinine higher than 1.3 mg/dL. The glomerular filtration rate showed that 80 (43.0%) patients presented creatinine clearance below 60 mL/min.

With regard to personal comorbities, the majority of patients had a history of Acute Myocardial Infarction or Angina Pectoris (133 - 71,5%), in 2nd place came those with Systemic Arterial Hypertension (124 - 66.7%), followed by diabetes mellitus in 29.6% (55 cases). Only 5 (2.7%) had undergone previous heart surgery.

Most patients (163 - 87.6%) had been undergone only CABG surgery, while others had been undergone CABG associated with valve repair (5.9%), left ventricular aneurysmectomy (4.9%) or correction of congenital heart disease (1.6%).

The mean age of patients who developed ARF was 62.8 ($\pm$ 9.4) years, comparing with 61.3 ($\pm$ 8.8) years in the group without ARF, with *P*-value = 0.293.

Univariate analysis of preoperative variables studied (age, gender, serum creatinine, history of diabetes, hypertension, myocardial infarction/angina and heart surgery), by comparing the groups of patients with and without ARF, there was no association of these informations collected with the event of renal failure in the postoperative period.

The time of cardiopulmonary bypass and aortic clamping were risk factors for postoperative complications associated with ARF, as shown in Table 1.

The evolution of serum creatinine in the postoperative period showed that values were higher in the group that developed ARF and statistically significant difference in the T1 to T4 interval was noted, when compared to the group with no ARF (Table 2).

In 149 medical records assessed there was information on the value of serum creatinine in the patient's discharge from the ICU, and 1.61 ($\pm$1.10) mg/dL on average for the ARF group and 1.05 ($\pm$0.41) mg/dL in the group without ARF, with *P*-value = 0.0004.

Regarding postoperative monitoring, we found that the average of the mean arterial pressure in the T1-T4 interval was almost equal in both groups, being 93.5 ($\pm$ 10.9) mmHg in the ARF group and 93.9 ($\pm$10.2) mmHg in patients without ARF, with *P*-value=0.792. The average diuresis was also similar between patients with and without ARF, respectively, as follows, 1.98 ($\pm$ 0.97) mL/kg/h and 2.06 ($\pm$0.81) mL/kg/h and *P*-value=0.561.

Qualitative variables related to postoperative monitoring are described in Table 3. The main complications presented in the postoperative period are described in Table 4. We highlight the fact that hypotension, bradycardia and arrhythmia have presented any statistical relationship with the occurrence of Acute Renal Failure.

After univariate analysis, a multivariate logistic model

Table 1.   Intraoperative variables of patients with and without ARF undergone CABG surgery.

Variables	ARF		without ARF		OR (CI 95%)	*P*
	N	%	N	%		
More than one procedure						0.483
Yes	9	15.8	14	10.9	1.54 (0.62 – 3.79)	
No	48	84.2	115	89.1	1.00	-
Duration of cardiopulmonary bypass						0.011
≥ 115 min	28	49.1	37	28.7	2.40 (1.26 – 4.57)	
< 115 min	29	50.9	92	71.3	1.00	-
Aortic clamping time						0.044
≥ 85 min	19	33.3	24	18.6	2.18 (1.07 – 4.43)	
< 85 min	38	66.7	105	81.4	1.00	-
Total of anastomoses						0.105
> 3	12	21.1	14	10.9	2.19 (0.94 – 5.09)	
≤ 3	45	78.9	115	89.1	1.00	-

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Table 2. Mean value of serum creatinine in the postoperative of
patients with and without ARF undergone CABG
surgery.

Period	ARF		without ARF		P
	Mean	N	Mean	N	
T1	1.39 (±0.47)	56	1.16 (±0.79)	117	0.043
T2	1.88 (±0.69)	55	1.23 (±0.37)	117	<0.0001
T3	1.79 (±0.96)	52	1.08 (±0.42)	113	<0.0001
T4	2.00 (±1.27)	29	1.04 (±0.37)	36	<0.0001

was built, which included only variables that were statistically significant (P-value <0.05). Data from the multivariate analysis are presented in Table 5.

The mortality rate found in the study was 3.2% (6/186). The number of deaths among patients with and without ARF was 5 (8.8%) and 1 (0.8%), respectively, with P-value=0.016 (OR=12.3, 95% CI 1.40 - 107.91). Among patients who required dialysis, mortality was 50.0% (2/4) and among patients who did not use dialysis was 5.7% (3/53), with P-value=0.035 (OR=16.7; 95% CI 1.70 - 162.96).

Table 3. Variables of postoperative monitoring of patients with and without ARF undergone CABG.

P	Variables	ARF		without ARF		OR (IC 95%)
		N	%	N	%	
<0.0001	ICU stay over 3 days					
	Yes	22	38.6	14	10.9	5.16 (2.39 – 11.14)
-	No	35	61.4	115	89.1	1.00
0.006	Mechanical ventilation over 24h					
	Yes	18	31.6	17	13.2	3.04 (1.42 – 6.48)
-	No	39	68.4	112	86.8	1.00
0.049	Need for IAB*					
	Yes	5	8.8	2	1,6	6.11 (1.15 – 32.48)
-	No	52	91.2	127	98.4	1.00
0.266	Diuresis <1mL/kg/h					
	Yes	7	12.3	8	6.2	2.11 (0.72 – 6.15)
-	No	50	87.7	121	93.8	1.00
0.0001	Use of inotropic drugs**					
	Yes	15	26.3	7	5.4	6.22 (2.37 – 16.30)
-	No	50	87.7	121	93.8	1.00

*IAB = Intraaortic balloon; ** Dobutamine or Dopamine after the T3 period*

Table 4. Postoperative complications in patients with and without ARF undergone CABG.

Variables	ARF		without ARF		OR (CI 95%)	P
	N	%	N	%		
Bleeding						0.108
Yes	9	15.8	9	6.9	2.50 (0.93 – 6.67)	
No	48	84.2	120	93.1	1.00	-
Bradycardia						0.002
Yes	6	10.5	0	0	NC*	
No	51	89.5	129	100	1.00	-
Hypotension						0.045
Yes	19	33.3	24	18.6	2.19 (1.08 – 4.43)	
No	38	66.7	105	81.4	1.00	-
Reoperation						0.162
Yes	3	5.3	1	0.8	7.11 (0.72 – 69.90)	
No	54	94.7	128	99.2	1.00	-
Arrhythmia						0.005
Yes	9	15.8	4	3.1	5.86 (1.72 – 19.92)	
No	48	84.2	125	96.9	1.00	-
Stroke						0.764
Yes	1	1.8	0	0	NC*	
No	50	87.7	129	100	1.00	-

NC = Non-calculated

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DISCUSSION

Studies such as those developed by Yeboah et al. [12] and Abel et al. [13], approaching the relationship between heart surgery and ARF have been published for over 30 years. Interest in this subject is due to the fact that the ARF is a frequent complication related to surgical procedures, especially cardiovascular surgeries, and is related to increased morbidity and mortality in the postoperative [14].

Table 5. Multivariate analysis of risk factor for ARF in patients undergone CABG.

Variables	OR (CI 95%)	P
Cardiopulmonary bypass		0.668
≥ 115 min	1.26 (0.43 – 3.72)	
< 115 min	1.00	-
Aortic clamping time		0.460
≥ 85 min	1.54 (0.48 – 4.87)	
< 85 min	1.00	-
Stay in ICU over 3 days		0.018
Yes	3.28 (1.22 – 8.84)	
No	1.00	-
Mechanical ventilation over 24h		0.521
Yes	0.68 (0.21 – 2.17)	
No	1.00	-
Need for IAB*		0.758
Yes	1.46 (0.12 – 17.06)	
No	1.00	-
Hypotension		0.942
Yes	103 (0.42 – 2.51)	
No	1.00	-
Arrhythmia		0.309
Yes	2.17 (0.48 – 9.67)	
No	1.00	-
Use of inotropic drugs**		0.455
Yes	1.74 (0.40 – 7.45)	
No	1.00	-

*IAB = Intraaortic balloon; **Dobutamine ou Dopamine after the T3 period.*

The prevalence of ARF found in our study was 30.6%, similar to that described by Kochi et al. [15], with 34.0%, in a study with 150 patients. In our case, we collected information from medical records of 186 individuals. Other studies, such as by Tuttle et al. [16] and Yehia et al. [3] presented higher prevalence than ours (41.3% and 42.0%, respectively). In the study by Santos et al. [2], Chertow et al. [9], Stallwood et al. [17] and Conlon et al. [18], the rates of ARF were 16.1%, 7.9%, 2.4% and 1.1% respectively, well

below those described in our group. Such differences can be explained by the different criteria for the definition of postoperative ARF used by the authors.

The use of dialysis is one of the criteria used to define ARF in the postoperative of heart surgery [2,18,19]. The need for dialysis is found in 0.7% to 30.6% of patients who develop acute renal failure in different publications [2,3]. In rare cases, as in the study published by Tuttle et al. [16], no patient developed ARF with the need for dialysis. Our study identified 7.0% of dialytic ARF, and risk factors for the event were not observed.

Most studies indicate the presence of previous impaired renal function as one of the factors associated with acute renal failure in the postoperative period of heart surgery [18]. The study by Walter et al. [20] pointed out the creatinine clearance estimated by Cockcroft-Gault method, as a more reliable indicator when compared to the value of serum creatinine, to determine the risk of unfavorable outcomes in the postoperative of heart surgery. In our study, as well as developed by Lobo [21], there was no relationship between preoperative creatinine clearance and poor outcome of renal function postoperatively.

Other preoperative variables such as advanced age, diabetes mellitus, previous heart surgery and arterial hypertension, which classically are described as risk factors for ARF in other publications, were not correlated with worsening of renal function among patients approached in this study perhaps by the number of patients studied herein was lower than that of other studies [2,17,18,22].

Among the surgical variables investigated, two were statistically related to the risk of development of ARF. The mean time of cardiopulmonary bypass (CPB) and aortic clamping were higher in the group with ARF (*P*-value <0.05). In the study by Regner et al. [19], which also assessed these two parameters, only the mean of the CPB showed significant relationship with the abrupt drop of renal function, unlike the study of Tuttle et al. [16], on which the two variables were statistically significant for evolution ARF in the postoperative period, with *P*-value <0.0001.

The changes caused by the use of cardiopulmonary bypass include contact with nonendothelial surfaces, the exclusion of pulmonary flow, the presence of continuous minimally pulsatile or nonpulsatile flow and the onset of endocrine-metabolic response is proportional to a major surgery, all this culminating in an inflammatory response not susceptible to external control [23]. The positive impact of the absence of CPB on renal function in postoperative of heart surgery can be observed in the study by Milani et al. [24], in which only 0.2% of patients developed ARF, a value less than that found in studies in which CPB was used [25,26]. In another study, developed by Lima et al. [27], assessing octogenarian patients undergoing CABG surgery, the presence of ARF was 19.2% in the on-pump

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group and none in patients without CPB.

With respect to the follow-up it was observed that in the group with ARF the mean serum creatinine was higher in the range T1 to T4 and at the time of discharge. In the study by Kochi et al. [15] the assessment of the mean value of serum creatinine, 24 and 48 hours after surgery, also showed higher values in the group with ARF (*P*-value <0.0001). According to the study by Ryckwaert et al. [28], minimum changes in the values of creatinine in the postoperative period are not rare events and have a significant impact on follow-up of patients with decreased survival.

Several studies indicate a relationship between ARF and length of hospital stay. This study assessed only the period of ICU stay, and staying for more than three days - that was the only variable that, after multivariate analysis, showed an association with ARF in the postoperative period. The study of Ryckwaert et al. [28] also pointed out the relationship between prolonged ICU stay and renal failure postoperatively.

The mean time of mechanical ventilation over 24 hours was higher in the ARF when compared to those without ARF (31.6% vs 13.2%, respectively, with *p*-value = 0, 006). Our result was consistent with that found by the study of Anderson et al. [29], in which the need for mechanical ventilation for more than 24 hours was higher among patients with poor evolution of renal function. Vieira et al. [30] assessing 140 patients admitted to the ICU at an oncology hospital, observed that the occurrence of ARF determined not only a longer duration on mechanical ventilation, but also it took a longer period of time to promote the disconnection from mechanical ventilation.

Two parameters that, according to Santos et al. [2], can indirectly assessing cardiac performance, were associated in our study to the development of ARF in the postoperative period. The need for intra-aortic balloon and inotropic drugs (dopamine or dobutamine), from the period T3, were higher among patients with ARF.

Among the postoperative complications investigated: bradycardia, hypotension and arrhythmia, such complications were related to worsening renal function of patients. The damaged cardiac function, creating a situation of low cardiac output, and therefore a presentation of hypoperfusion, may precipitate pre-renal ARF, which if not promptly corrected, can evolve into the intrinsic ARF and even cortical necrosis, a situation that results in an irreversible presentation of loss of renal function [14].

Acute renal failure is considered an independent risk factor for death in the postoperative period of heart surgery. The mortality reported in the literature ranges from 14.5% to 63.7% [2,9,31,32]. In our study, mortality among patients with ARF was only 8.8%, lower than that found by other authors. This can be explained, in part, because the surgical procedures included in this study were all elected, with patients in better clinical condition before surgery.

CONCLUSIONS

1 - The cardiopulmonary bypass time (>115min), aortic clamping time (>85 min), need for intra-aortic balloon, mechanical ventilation for more than 24 hours, bradycardia, hypotension, arrhythmia and the need for inotropic drugs were considered risk factors for ARF;

2 - The presence of renal failure was correlated with a worse postoperative outcome, characterized by longer stay in Intensive Care Unit and higher mortality.

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