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Acute kidney injury in the postoperative period of cardiac surgery

Lesão renal aguda no pós-operatório de cirurgia cardíaca

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Abstract

Objective: To identify the occurrence of acute kidney injury (AKI) in the postoperative period of cardiac surgery.
Methods: A prospective cohort study including 51 patients exposed to coronary artery bypass surgery, valve replacement, or combined surgery (bypass surgery and valve replacement) without history of kidney disease and kidney transplant, and who were followed from the preoperative period until 72 hours after surgery. Acute renal failure was defined as baseline creatinine increase of 0.3 mg/dL in 48 hours or less, or its increase from 1.5 to 1.9-fold, or a reduction in urine flow <0.5mL/kg/h for 6 hours. The Kidney Disease: Improving Global Outcomes (KDIGO) classification was used.
Results: The KDIGO classification showed that 92.2% of patients had renal impairment. The urinary flow criterion of this classification alone showed that 31.4% of patients had renal dysfunction in stage of risk, 33.3% in stage of renal injury, and 21.6% in stage of renal failure. By the serum creatinine criterion, 27.5% were identified in the stage of risk, 3.9% in stage of injury and another 3.9% in stage of kidney failure.
Conclusion: A high percentage of patients in the postoperative period of cardiac surgery (coronary artery bypass surgery and valve replacement) progressed to acute kidney injury.

Resumo

Objetivo: Identificar a ocorrência de lesão renal aguda em pós-operatório de cirurgia cardíaca.
Métodos: Estudo de coorte prospectivo que incluiu 51 pacientes expostos a cirurgia de revascularização do miocárdio, troca valvar ou cirurgia combinada (revascularização do miocárdio e troca valvar), sem antecedentes de doença renal e de transplante renal e que foram acompanhados desde o pré-operatório até 72 horas de pós-operatório. Foi definido como lesão renal aguda o aumento de 0,3mg/dL em tempo menor ou igual a 48 horas ou aumento de 1,5 a 1,9 vez da creatinina basal, ou ainda redução do fluxo urinário <0,5mL/kg/h por 6 horas. Foi utilizada a classificação *Kidney Disease: Improving Global Outcomes* (KDIGO).
Resultados: A classificação KDIGO sinalizou 92,2% dos pacientes com disfunção renal. O critério fluxo urinário dessa classificação isoladamente mostrou que 31,4% dos pacientes apresentaram disfunção renal no estágio de risco, 33,3% no estágio de lesão renal, e 21,6% no estágio de falência renal. Pelo critério creatinina sérica, foram identificados 27,5% no estágio de risco e, nos estágios de lesão e falência renal, foram identificados 3,9% pacientes em cada.
Conclusão: Um percentual elevado de pacientes em pós-operatório de cirurgia cardíaca (revascularização miocárdica e troca valvar) progrediu com lesão renal aguda.

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Introduction

Acute kidney injury (AKI) is considered an abrupt, potentially reversible condition, and generally with complete recovery when the patient survives this stage of disease.[1]

However, recent epidemiological and observational studies highlight the association of an episode of acute kidney injury with long-term adverse outcomes such as chronic kidney disease, cardiovascular events and premature death. The increased incidence of acute kidney injury and its association with severe intra-hospital complications, coupled with rising costs, are factors that make this disease a major problem for health systems.[1]

Acute kidney injury is a clinical syndrome broadly defined as an abrupt decline in renal function, which occurs over a period of hours to days and results in retention of nitrogen products and metabolic waste. Although its initial clinical manifestation is usually oliguria, the volume of urine may be normal or high, and patients may be asymptomatic, especially in the beginning of the clinical picture. The diagnosis of acute kidney injury is revealed from a recent increase in serum creatinine and/or urea, or a reduction in urine output.[2]

Risk factors for acute kidney injury include older age, male gender and diabetes mellitus.[3] However, the most important risk factor is the pre-existing chronic kidney disease.[4] This, in turn, is a predictor of acute kidney injury in the postoperative period.[5]

Acute kidney injury is a critical problem in severely ill patients and is usually predictive of increased morbidity and mortality.[6] It affects between 5 and 30% of patients in the postoperative period of cardiac surgery.[7,8]

Renal dysfunction can be identified in the postoperative period of cardiac surgery, both in patients with pre-existing renal damage and in those without previous renal impairment. Thus, in this period, the mortality from acute kidney injury increases substantially.[9]

The need to diagnose acute kidney injury as early as possible, in order to prevent or limit the various complications associated with it, has become the key for implementing strategies to control and minimize the risks of progression to chronic kidney disease.[10]

In this scenario, the standardization of diagnosis and staging of acute kidney injury has become a worldwide effort in the development and improvement of multidimensional classification systems sensitive to the detection and stratification of renal injury. Among these, stand out the RIFLE criteria (acronym from Risk, Injury, Failure, Loss in End-stage) and Acute Kidney Injury (AKIN), published in 2004 and 2007, respectively.[11]

Despite the current achievements, the mortality rate has barely changed, which has maintained and made the deployment of tools for the early identification of AKI an urgent matter. Based on the RIFLE and AKIN classifications, in 2012 the classification named Kidney Disease: Improving Global Outcomes (KDIGO) was published and implemented in clinical and surgical realities for identifying its diagnostic value and its precocity in the identification of acute kidney injury in hospitalized patients.[2,12]

The KDIGO classification (Chart 1) can subsidize the early management of patients in clinical practice by defining the AKI as the serum creatinine increase of 0.3mg/dL in a 48-hour period and/or reduction of glomerular filtration rate (GFR) in 7 days, or even the urine output reduction lower than 0.5 mL/kg/h for 6 hours. Serum creatinine and urine output are key markers for renal impairment staging.[12]

Chart 1. *Clinical Practice Guideline for Acute Kidney Injury*

KDIGO Classification	
Stage 1 (risk)	Increase in baseline creatinine between 1.5 and 1.9-fold, or increase of >0.3 mg/dL, or decreased urine output <0.5mL/kg/h for 6 to 12 hours
Stage 2 (renal injury)	Increase in baseline creatinine between 2 and 2.9-fold, or decreased urine output <0.5mL/kg/h for more than 12 hours
Stage 3 (renal failure)	Increase in baseline creatinine of 3-fold, or creatinine increase to >4mg/dL, or start of dialysis, or in patients under 18 years, estimated creatinine clearance <35mL/min/1,73m² or decreased urine output <0.3mL/kg/h for more than 24 hours, or anuria for 12 hours or more

Adapted: Kidney Disease Improving Global Outcomes (KDIGO). Clinical Practice Guideline for Acute Kidney Injury. Kidney Int. 2012.

In this scenario, studies have shown that active surveillance of changes in serum creatinine and urine output can automate alerts, guide the dosing of drugs, reduce the incidence of acute kidney injury, improve patient safety and help with identifying the occurrence of complications.[13,14]

The objective of this study was to identify the occurrence of acute kidney injury in the postoperative period of cardiac surgery.

Methods

This is a cohort, prospective and quantitative study carried out from August 2013 to June 2014 in the intensive care unit of a public hospital in Distrito Federal.

Patients aged over 18 years, exposed to coronary artery bypass surgery, valve replacement, or combined surgery (bypass surgery and valve replacement) without history of kidney disease and kidney transplantation were included. Those exposed to surgery of aneurysm correction, vascular surgery, contrast examinations in the last 72 hours prior to surgery and with chronic kidney disease (glomerular filtration rate<60mL/min/1.73m^2) were excluded.

To obtain the estimation of the sample size (n) was used a ratio estimator formula. The p-value considered in the formula was 85%, obtained from patients who developed acute kidney injury in a pilot test with 20 patients. For the formula parameter, was assumed the absolute precision (d) of d = 10%. The sample size calculation resulted in 49 patients. The sample size used was 51 patients.

The follow-up of patients was from the preoperative period until 72 hours after surgery and was linked to the exposure to cardiac surgery procedure.

Acute renal failure was defined as baseline creatinine increase of 0.3 mg/dL in 48 hours or less, or its increase of 1.5 to 1.9-fold, or a reduction in urine flow <0.5mL/kg/h for 6 hours.[12]

Data were collected from a structured data collection instrument with information of identification, demographic, clinical (previous diseases, use of medicines and pre-surgery laboratory tests), surgical (time of surgery, use of vasoactive drugs, intubation time, post-surgery laboratory tests and type of surgery), length of stay in the intensive care unit, and the prognostic index called Acute Physiology and Chronic Health Evaluation II (APACHE II).

The results were expressed in absolute and relative frequency, median and percentile of 25% and 75%. The Fisher's exact test and chi square test were used for analysis of categorical variables. The Mann-Whitney test was used to compare categorical and continuous variables, and the Spearman's rank correlation coefficient was calculated to compare the continuous variables. P-values <0.05 were considered significant.

The development of the study met national and international ethical standards for research involving human beings.

Results

In total, 51 patients with average age of 58±17 years were followed-up in the study. The majority (58.8%) was hypertensive, with mean body mass index of 25,9kg / m2 and APACHE II of 15. There was a slight predominance (51%) of the female gender and the majority of patients used vasoactive drugs (Table 1).
A percentage of 21.6% of patients had surgical procedures prior to cardiac surgery. Among cardiac surgeries, there was prevalence of coronary artery bypass, followed by valve replacement and, the combined surgeries in a lesser percentage. The mean duration time of surgery was 300 minutes. The patients remained on mechanical ventilation for a median period of 12 hours. The positive end-expiratory pressure (PEEP) average of these patients was 5.4cmH2O (Table 1).

The cardiopulmonary bypass (CPB) time in valve replacement surgery was superior to the time in coronary artery bypass surgery.

The KDIGO classification signaled 92.2% of patients with renal impairment. The urinary flow criterion of this classification alone showed that 31.4% of patients had renal dysfunction in stage of risk, 33.3% were classified in the stage of renal injury and 21.6% in stage of renal failure. By the serum creatinine criterion, 27.5% were identified in the risk stage and 3.9% in both the stages of renal injury and renal failure.

There was a significant relationship between the male gender and performing coronary artery bypass surgery (p = 0.04) by the chi square test. The patients who underwent valve surgery (29.4%) made more use of vasopressin, and this statistical relationship was significant (p = 0.007) by the Fisher's exact test.

Table 1. Distribution of patients according to clinical characteristics

Characteristics (n=51)	n(%)	Mean (±SD)	Median (25%-75%)
Age (years)	-	58±17	-
Female gender	26(51.0)	-	-
BMI* (kg/m²)	-	25.9±4.7	-
Use of vasoactive drugs	-	-	-
Dobutamine	40(78.4)	-	-
Noradrenaline	33(64.7)	-	-
Vasopressin	4(7.8)	-	-
APACHE II*	-	-	15 (12-18)
Surgery*		-	-
Coronary artery bypass surgery	33(64.7)	-	-
Valve replacement	15(29.4)	-	-
Combined	2(3.9)	-	-
Duration of surgery (minutes)**	-	-	300 (240-360)
Ventilation time (hours)***	-	-	12 (8-20)
PEEP****	-	5.4±0.9	-
Renal impairment	47(92.2)	-	-
CPB time (minutes)			
Valve replacement			123 (93-153)
Coronary artery bypass graft surgery			90 (70-101)
Comorbidities	-	-	-
Hypertension	30(58.8)	-	-
Diabetes	19(37.3)	-	-
Smoking	19(37.3)	-	-
Dyslipidemia	12(23.5)	-	-

*50 patients with data; **46 patients with data; ***47 patients with data;****48 patients with data. SD – Standard Deviation; BMI – Body Mass Index; APACHE II – Acute Physiology and Chronic Health Evaluation II; PEEP – Positive End-Expiratory Pressure; CPB – Cardiopulmonary Bypass

A significant relationship was found between the coronary artery bypass surgery and the following risk factors: hypertension (p = 0.04), diabetes (p = 0.001), smoking (p = 0.008) and dyslipidemia (p = 0.009), according to the chi square test.

Patients undergoing coronary artery bypass surgery had median age between 51 and 73 years, and those who underwent valve surgery between 35 and 55 years. These results showed significant association (p<0.001) by the Mann-Whitney test. On the other hand, the body mass index was similar among patients undergoing coronary artery bypass surgery (26.6) and valve replacement (25).

Patients who underwent coronary artery bypass surgery showed a higher percentage (61.5%) of kidney injury or failure, while among those who underwent valve replacement, a lower percentage (38.5%) progressed to kidney injury or failure.

Regarding the surgical scenario, patients who underwent valve surgeries required longer time of cardiopulmonary bypass, between 93 and 153 minutes and, consequently longer surgical time (340 minutes), compared to those who underwent coronary artery bypass surgery, in which surgical time ranged from 70 to 101 minutes, and 270 minutes of surgery. In particular, the CPB time was significantly associated with the type of surgery (p = 0.01), but this association was not observed with surgical time (p = 0.1).

Discussion

Limitations of this study were related to absolute increases in serum creatinine by acute changes in the volume of distribution, acute dehydration or situations of volume expansion, which are common in critically ill patients hospitalized in intensive care units.[15] In addition, the adopted sample size can also limit the generalization of results. On the other hand, the study contributes to encouraging the health team to use a functional classification for identification of acute kidney injury, especially nurses, who are the professionals responsible for direct management of patients.

Acute kidney injury is a complication often observed in the postoperative period of cardiac surgery, with complex clinical repercussions that impact negatively on the early and late prognosis of patients.[16] Despite the scientific and technological advances in the health field, the approach of acute kidney injury is complex and challenging due to lack of criteria for its classification of complexity and early identification.[17,18] Thus, implementing the KDIGO classification system enabled the recognition and stratification of acute kidney injury in the intensive care setting.

This functional classification system of the kidneys is of fundamental importance and favors the monitoring of renal function, facilitating the implementation of measures for prevention and treatment of early acute kidney injury.[10,19]

The female gender was identified as an independent risk factor for postoperative renal injury, although this is not a consistent finding. However, compared to men, women normally have less muscle mass and are typically older at the time of surgery. These two factors can affect serum creatinine levels. In this study, the female gender was predominant and such evidence can be a factor to justify the significant percentage of renal injury, considering that women have physiologically lower glomerular filtration rates than men.[20] Allied to this factor, the use of potent vasoconstrictor drugs (norepinephrine and vasopressin) in a percentage of patients in this study may be an aggravating additional for kidney dysfunction.

Acute kidney injury is known to be multifactorial. However, one of the most common causes of acute kidney injury in patients who underwent cardiac surgery is resultant of the perfusion techniques used in extracorporeal circuit management. Such techniques can trigger the need for dialysis or renal replacement therapy. A meta-analysis showed that off-pump surgery may decrease the risk of acute kidney injury compared to cardiopulmonary bypass surgery. Nonetheless, these results were inconclusive, considering the several definitions of this pathology.[19]

Moreover, during cardiac surgery, generally it is not the extracorporeal circulation alone, but also its duration time that causes a reduction in kidney function. The duration of cardiopulmonary bypass and the occurrence of postoperative renal dysfunction are controversial. However, a meta-analysis found that this period represents an independent risk factor for acute kidney injury.[18] In this sense, the present study found a statistically significant relationship ($p = 0.01$) between the type of surgery and cardiopulmonary bypass time.

Patients with AKI generally have longer periods of hospital stay and consume more financial resources. In accordance with current evidence, few markers determine if the kidneys are adequately protected during surgery.[21]

Scientific evidence identified acute kidney injury incidences of 14 and 51% using the KDIGO classification system.[22,23] However, in this study, more than half of patients developed acute kidney injury after cardiac surgery. Among other factors, this is because the classification enables the identification of acute kidney injury in the first two days after renal insult.[24]

In addition, it was found that a high percentage of patients progressed to stage 2. In this context, the importance of implementing protocols, warning systems and preventive strategies should be reinforced in clinical practice, in order to control the impact of this insult in the quality of life of affected individuals, minimize the risk of progression to more advanced stages of disease and worsening of prognosis.[21]

Decreased urine output can determine hemodynamic and endocrine changes, but not all the acute kidney injury is manifested through reduction of this parameter. Evidences have shown urine output as a more sensitive indicator to detect acute kidney injury than the biomarkers usually employed in clinical practice.[9,17]

Serum creatinine is a late marker of acute kidney injury. Changes in its results may be due to non-renal variables such as age, body weight, muscular mass, protein intake, among others, usually found late. From this perspective, the use of KDIGO classification subsidizes the early detection of acute kidney injury, and enables the staging of the degree of impairment of renal function.[17]

Advanced age, overweight and comorbidities are clinical characteristics of a population predisposed to the development of renal dysfunction.[9,17] Scientific studies such as the present one have showed that older age and overweight were factors present in the sample who developed AKI.[10,25]

The high APACHE II score can be considered a risk factor for death in patients with acute kidney injury, as well as risk for requiring dialysis[6] - a reality observed in this study.

Norepinephrine is used in cases of hypotension. In such cases, it is common that patients in the period after cardiac surgery develop acute kidney injury by reduction in renal blood flow and subsequently, ischemia. The major cause for the emergence of acute kidney injury after cardiac surgery is surely ischemia secondary to renal hypoperfusion.[26]

Scientific research shows that a higher time of mechanical ventilation significantly exposes patients to the occurrence of acute kidney injury after cardiac surgery.[19] In this study, despite the high incidence of acute kidney injury, the invasive ventilation strategy employed an average positive end-expiratory pressure of $5.4 \pm 0.9 cmH_2O$. A systematic review supported that the occurrence of acute kidney injury in patients on invasive mechanical ventilation was more directly related to the change of hemodynamic variables. Still, the possibility of developing this pathology as a result of ventilation strategy is not excluded.[27]

The KDIGO classification favors the early identification of kidney dysfunction and thus, enables the adoption of preventive measures and implementation of individualized interventions to identify renal impairment, which may represent an important differential in clinical practice.

Conclusion

A high percentage of patients in the postoperative period of cardiac surgery progressed to acute kidney injury. Only by the urinary flow criterion of KDIGO classification, most patients were stratified in stages 1 or 2. The urine output showed greater discriminatory power as a marker of acute kidney injury when compared to the creatinine criterion.

Collaborations

Silva AVE participated in the design and development of the project. Nascimento MS and Aguiar TC participated in the collection and interpretation of data and writing of the article. Duarte TTP contributed in the stages of study review, formatting, organization of theoretical framework, correction of agreement and submission process. Magro MCS collaborated in the stages of design, project planning, analysis and interpretation of data, writing and critical review of important intellectual content and approval of the final version to be published.

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