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## Evaluation of the renal function in patients in the postoperative period of cardiac surgery: does AKIN classification predict acute kidney dysfunction?

*Avaliação da função renal em pacientes no pós-operatório de cirurgia cardíaca: a classificação AKIN prediz disfunção renal aguda?*

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### ABSTRACT

**Objectives:** To identify the frequency of the Acute Kidney Injury and to compare the application of the AKIN classification with the separate use of the serum creatinine in the postoperative period of cardiac surgery.

**Methods:** This study was prospectively developed in a teaching and specialized research hospital in cardiology of the public health system of the state of São Paulo. Forty-four patients submitted to the elective cardiac surgery since the immediate post-surgical period up to the 2<sup>nd</sup> post-surgical period were followed.

**Results:** It was possible to verify that from the forty-four patients, 75% were hypertensive, 27% were diabetic and mostly were male (64%), with an average age of 55+16 years old. It was observed that advanced age and the elevated body mass index shows a significant correlation to renal dysfunction ( $p < 0,05$ ). Accord-

ing to the AKIN classification, the urinary flow criterion identified more renal dysfunction than creatinine criterion. It was verified that the renal dysfunction occurred more frequently in the post-surgery period and the majority (82%) from the 63,6% of the patients which were submitted to the revascularization of the myocardium surgery.

**Conclusion:** The majority of patients (75%) evolved initially with renal dysfunction signaled it mainly by the urinary flow criterion from the AKIN classification, a higher number compared to the separated creatinine. This fact confirms that the serum creatinine association with the urinary flow has a higher discriminatory performance for the early identification of this syndrome comparatively with the routinely use of the isolated creatinine.

**Keywords:** Kidney/ injuries; Biological markers; Cardiac surgery; Postoperative period; Creatinine

### INTRODUCTION

The acute kidney injury (AKI) is considered a severe complication of an enormous magnitude in the cardiac surgery post operative period not only by the impact in morbidity and mortality but also for the prolonged hospital stay.

The term AKI has a restrict use for patients with acute renal dysfunction without the need of a substitutive renal therapy. When the renal injury imposes the need of the use of the substitutive renal therapy, the utilized denomination remains acute renal failure (ARF).<sup>(1)</sup>

The AKI affects about 1% to 25% of the critically ill patients<sup>(2,3)</sup> depending on the criterion used to define it. In the cardiac surgery this number can achieve around 5% to 30% of the post operative patients and it is related to a higher risk of mortality (up to 80%).<sup>(4-8)</sup>

In the last years, AKI prevention strategies have been emphasized aiming to

minimize risks, since its most used common markers in the clinical practice show late and low sensibility in a general way which usually delays the decision making related to appropriate therapeutics. Recently, the application of new biomarkers which shows earlier not only the presence of the renal injury but also the its affected site has been stimulated, so that the recovery occurs faster. It was confirmed that the evaluation of the renal function should not be restricted only to the use of a single biomarker. Many markers have been made and currently are being investigated, but until now there is no consensus about which one has a better diagnostic power.

It is considered that the lack of an exact identification of the occurrence of AKI may be related to the absence of consensus in its definition. In this case, the standardization of a concept of AKI with the objective to homogenize conducts and enable a comparison between studies, beyond to provide therapeutic interventions more appropriate with a better prognostic value, are initiatives which have become imperative.

In 2005, the classification Risk, Injury, Failure, Loss and End-Stage Renal Failure (RIFLE) has been redrafted by the "Acute Kidney Injury Network" (AKIN) (Chart 1),<sup>(9,10)</sup> with the proposal to clarify and anticipate the detection of acute renal injury. The AKIN classification is not a diagnosis, but a system of stratification of renal function which uses the worse value of serum creatinine and urinary flow. Beyond to represent an interesting proposal of systematization of the AKIN, it may be considered an advance in its definition. This proposal ensures and extends the odds of control of the syndrome, even before its manifestation.

The proposal of this study was expressed by the difficulty of evaluation and diagnosis of the AKIN by the method of serum creatinine routinely used nowadays. The AKIN classification, beyond to adopt the serum creatinine as a marker of renal injury, also uses the urinary flow, a

clinical indispensable measurement in the evaluation of renal function; considering that its alteration is not always related to the AKIN. This classification strengthens the standardization of the concept, proposes a system of early identification of the AKIN and ensures the individuality in the therapeutic approach.

Therefore, the objectives of this study were to identify the frequency of acute renal injury in patients in the post operatory cardiac surgery period and to compare the clinical application of the AKIN classification with the separated use of serum creatinine in daily evaluation of the renal function.

## METHODS

### Design

Longitudinal and prospective study, developed in a large cardiology hospital, located in the state of São Paulo, in surgery intensive care units from December 2006 to March 2007.

### Casuistic

The sample of this study was composed of forty-four patients with age between 18 and 65 years old, submitted to cardiac elective surgery of myocardial revascularization, valvar or combined surgeries.

### Exclusion criteria

The patients excluded from this study were those submitted to congenital cardiac surgery; patients with renal injury at the preoperative period (serum creatinine higher than 1.4 mg/dl), as adopted in the institution; patients with changes of the level of conscience and cognition or those using radiocontrast within 72 hours prior to surgery.

### Data collection operation

The study was approved by the Ethics Committee of

**Chart 1 – Classification system and stages of the acute renal injury**

Stage	Serum creatinine criterion	Urinary flow criterion
1	Increased serum creatinine $\geq 0.3$ mg/dl or increase for $\geq 150\%$ to $200\%$ (1.5X to 2x) of the basal value	$< 0.5$ ml/kg/h in $> 6$ h
2	Increased serum creatinine for $> 200\%$ to $300\%$ ( $>2x$ to $3x$ ) basal value	$< 0.5$ ml/kg/h in $> 12$ h
3*	Increased serum creatinine for $> 300\%$ ( $> 3x$ ) basal value, or serum creatinine $\geq 4.0$ mg/dl with an acute increase of at least $0.5$ mg/dl	$< 0.3$ ml/kg/h in 24h, or anuria for 12h

Acute renal injury is defined with an abrupt decrease (within 48 hours) of the renal function, currently defined by an absolute increase in serum creatinine levels  $\geq 0.3$  mg/dl, a percentage increasing in serum creatinine levels of  $\geq 50\%$  (1.5X basal value), or a decrease in urinary flow (registration oliguria  $< 0.5$  ml/kg/h in  $> 6$ h). \*Individuals which receive renal replacement therapy are considered in stage 3 without concerning to the stage on which they are at the time of renal replacement therapy.

Adapted from: Lopes JA, Fernandes P, Jorge S, Gonçalves S, Alvarez A, Costa and Silva Z, et al. Acute kidney injury in intensive care unit patients: a comparison between the RIFLE and the Acute Kidney Injury Network classifications. Crit Care. 2008;12(4):R110.

the institution and all participants signed the free and informed consent statement.

The data collection was performed via an instrument containing the demographic, clinical, surgical and biochemistry laboratory data, collected in medical records of each patient. The laboratorial biochemistry used in the data collection comprises the examinations that are routinely collected in surgery intensive care units, where the study was developed.

Acute renal injury was defined according to the AKIN classification, using the serum creatinine and urinary flow as criteria for evaluation of renal function. The application of the AKIN classification was performed in the immediate postoperative periods, 48 hours and 72 hours after the surgery for stratification of patients in renal dysfunction stages according to the degree of the organ involvement. Patients were classified into: 1<sup>st</sup> stage, 2<sup>nd</sup> stage and 3<sup>rd</sup> stage.

#### Treatment of data

The patients classified in stages 1, 2 or 3 were considered with “dysfunction”, contrasting with the normal patients.

The analysis of categorical variables was made by the Pearson’s chi-square test or Fisher’s exact test. The data were expressed in absolute frequency (n) and relative frequency (%). The analysis of the continuous variables was performed via the non-parametric Kruskal-Wallis test. The data were expressed as median and 25-75 percentiles. P values < 0.05 were considered significant.

## RESULTS

Forty-four patients were followed, with mean age of 55+16 years old, being most of them hypertensive (75%) and males (64%). The diabetics comprised 27% of the sample (Table 1).

The majority of patients with hypertension (81.8%) and diabetes (91.7%) evolved with renal dysfunction (Table 1), but there was no significant relationship between these variables. Patients with obesity and advanced age showed a higher prevalence of renal dysfunction (Table 1, p<0.05).

Table 2 showed that according to AKIN classification, there was a higher frequency of patients with renal function involvement identified by the urinary flow criterion than the creatinine one.

A greater distribution of patients with renal dysfunction involvement at the 1<sup>st</sup> postoperative day (PO) (65.9%) was observed. In the immediate post operative period (IPOP) and in the 2<sup>nd</sup> PO the frequency of involved patients was lower (36.4% and 38.6%, respectively), suggesting a trend towards function recovery from the 2<sup>nd</sup> PO (Figure 1). These data were confirmed in figure 2, represented by a greater frequency of patients with elevation in serum creatinine levels in the 1<sup>st</sup> OP and trend toward a reduction from the 2<sup>nd</sup> PO.

Stratifying the AKIN classification by the type of surgery, a significant percentage of patients (38.6%) submitted to myocardial revascularization evolved for stage 2 and 13.6%, evolved for stage 1. Among the patients submitted to heart valve surgery, 13.6% evolved for stage 2 and 6.8% were classified in stage 1. Only one patient (2.3%) was submitted to combined surgery and evolved for stage 2 (Figure 3).

**Table 1 - Clinical characteristics of global population and of the subgroups**

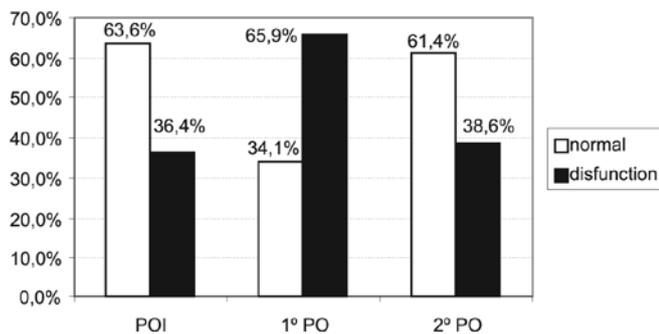
Characteristics	Global	Normal (n=11)	With dysfunction (n=33)	P-Value
Age (years)	55 ± 16	32 (23 - 59)	56 (53 - 67)	0.014
Male	28 (63.6)	6 (54.5)	22 (66.7)	0.35
BMI (kg/m <sup>2</sup> )	26.0 (23.3 - 29.8)	23.3 (22.5 - 24.2)	28.1 (24.2 - 31.8)	0.001
Hypertension	33 (75.0)	6 (54.5)	27 (81.8)	0.08
Diabetes	12 (27.3)	1 (9.1)	11 (33.3)	0.11

BMI - body mass index. Results expressed in ± average, standard deviation, median (25% - 75%) or n (%).

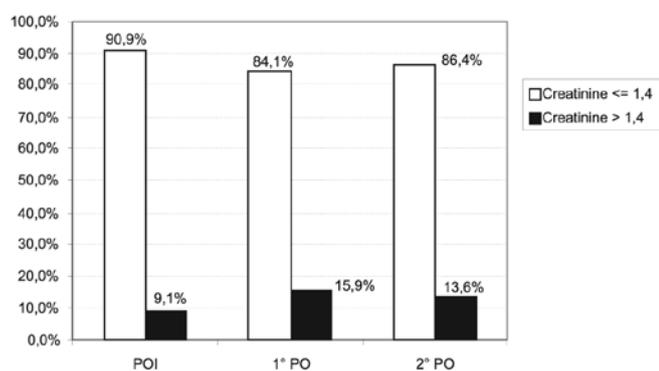
**Table 2 - Distribution of the patients in renal dysfunction stage according to the AKIN classification**

Stage	Urinary flow criterion	Serum creatinine criterion	AKIN classification
Normal	12 (27.3%)	34 (77.3%)	11 (25.0%)
1	8 (18.2%)	10 (22.7%)	9 (20.5%)
2	24 (54.5%)	0 (0.0%)	24 (54.5%)
3	0 (0.0%)	0 (0.0%)	0 (0.0%)

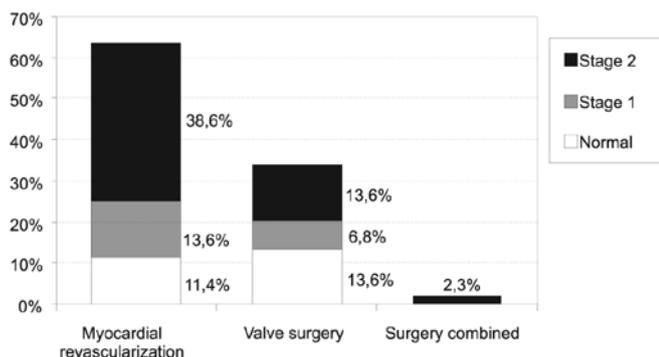
Results expressed in n (%).



**Figure 1 – Distribution of patients according to the AKIN classification in immediate post operative period (IPOP) (24 hours), 1<sup>st</sup> post operative (PO) (48 hours) and 2<sup>nd</sup> post operative (72 hours) post operative cardiac surgery.**



**Figure 2 – Distribution of patients according to the serum creatinine in immediate post operative (IPOP) (24 hours), 1<sup>st</sup> post operative (PO) (48 hours) and 2 post operative (72 hours) post operative cardiac surgery.**



**Figure 3 – Distribution of patients in stages of renal dysfunction according to the AKIN classification whereas the type of surgery.**

## DISCUSSION

Cardiac surgery usually has its results influenced by clinical characteristics of the patients, as well as by aspects inherent to surgical procedure and to extracorporeal

circulation.<sup>(11,12)</sup> Despite all the available interventionist technological development, nowadays the intensive care patients, comparing to those from 10-15 years ago, are older and are more ill. Consequently they can accumulate more co morbidities which sometimes commit the prognosis and delays recovery.

The progressive increasing of the incidence of acute renal injury in patients with advanced age has been checked by various researchers<sup>(13,14)</sup> and is also detached in a significantly way ( $p=0.014$ ) in this study.

One aspect frequently neglected in renal function for the elderly concerns to repercussions determined by frequent co morbidities common for this age group, such as hypertension, diabetes mellitus, atherosclerosis, cardiac insufficiency.<sup>(15,16)</sup> In this study the renal dysfunction involved most of the hypertensive and diabetic ones, although there was no significant relation ( $p=0.08$  e  $0.11$ , respectively).

The prevalence of obesity has increased drastically over these two decades.<sup>(17)</sup> According to Jong,<sup>(18)</sup> it represents a risk factor for progressive loss of renal function in patients with known kidney disease, and there is also evidence that obesity can compromise the kidney even in patients with a normal renal function. Condition detached in this study, by means of the significant relationship established between the higher body mass index (BMI) with the occurrence of renal dysfunction.

Acute renal injury is a complication quite common in the cardiac surgery post operative and its repercussion has admittedly acquired relevance in the last years by representing an independent risk factor for mortality.<sup>(19-24)</sup>

A short time ago, the application of serum creatinine for evaluation of renal function as diagnostic marker was decisive,<sup>(2,4-7,25-30)</sup> but the vast range of its values for determining the renal injury was one of the greatest difficulties to standardize the diagnosis of this syndrome.

The absence of early biomarkers applied in clinical practice stimulated the insertion of urinary flow as evaluation of renal function, beyond to the serum creatinine routinely used. This innovation in the evaluation of renal function arose with the advent of RIFLE Classification, currently modified by the “Acute Kidney Injury Network” (AKIN) in order to make an even early identification of renal dysfunction.

Evidently, the urinary flow may vary as a direct consequence of endocrine changes, renal perfusion pressure and obstructive etiologies among others. However, according to Bellomo,<sup>(31)</sup> the urinary flow is more sensitive than biochemical markers for signs of change in the renal hemodynamic, a fact also verified in this study where the urinary

flow criterion had identified more renal dysfunction than the criterion creatinine.

Despite that, according to Lin,<sup>(32)</sup> the urinary flow is still a variable not yet well studied in cardiac surgery post operator, although it reveals a greater sensitivity to changes in renal function than the biochemical markers. It is less specific, except in situations in which is significantly reduced or absent. So this is the importance demonstrated in the RIFLE proposal and confirmed by the AKIN classification, not only of the use creatinine excretion, but also of urine production,<sup>(33)</sup> in an attempt to increase the capacity to optimize and adjust the treatment of patients with renal dysfunction.

Each year, approximately 600,000 patients, submitted to myocardial revascularization surgery with cardiopulmonary bypass, suffer physiologic modifications that determine ischemia and infarction of several systems.<sup>(34-36)</sup> It is known that the non-pulsatile blood flow increases the levels of circulating catecholamines and inflammatory mediators and the release of free hemoglobin from traumatized erythrocytes result in numerous answers in the renal physiopathology.<sup>(37-39)</sup> In this study, the changes in renal hemodynamic determining renal dysfunction itself occurred predominantly in the 1<sup>st</sup> PO, in patients submitted to myocardial revascularization with a tendency to stabilization from the 2<sup>nd</sup> post operator (72 hours).

In such case, as confirmed by numerous studies,<sup>(40-42)</sup> patients submitted to cardiac surgery in a general way may develop a bad distribution of renal blood flow, an increasing renal vascular resistance and substantive decrease (25 to 75%) of the renal blood flow and of the glomerular filtration rate.<sup>(25)</sup> So it confirmed a significant frequency of renal dysfunction in patients submitted primarily to cardiac surgery, detached in this study by the myocardial revascularization (52.2%). According to some studies<sup>(43,44)</sup> the group of higher risk in developing AKIN is submitted to combined surgery (myocardial revascularization and valve), with an incidence of 2.3% also checked here.

## CONCLUSION

The majority of patients (75%) developed renal dysfunction in the first 72 hours of post operator, using the

AKIN classification.

The AKIN classification had demonstrated to be a useful instrument in the evaluation of renal function in the post operator period, mainly by the presence of urinary flow as an evaluation of renal function.

The post operator myocardial revascularization surgery presented a higher prevalence for renal dysfunction.

The results suggest that the use of the AKIN classification in clinical practice may be a differential for evaluation and diagnosis of ARI and, therefore, contribute to early adoption of interventions in the post operator cardiac surgery period.

## RESUMO

**Objetivos:** Identificar a frequência de lesão renal aguda e comparar a aplicação da classificação AKIN com o uso isolado da creatinina sérica no pós-operatório de cirurgia cardíaca.

**Métodos:** Este estudo foi desenvolvido prospectivamente em um hospital de ensino e pesquisa especializado em cardiologia da rede pública do estado de São Paulo. Foram acompanhados 44 pacientes submetidos à cirurgia cardíaca eletiva, desde o pós-operatório imediato até o 2º pós-operatório.

**Resultados:** Constatou-se que dos 44 pacientes, 75% eram hipertensos, 27% diabéticos e eram majoritariamente do sexo masculino (64%), com média de idade de 55±16 anos. Observou-se que a idade avançada e o índice de massa corpórea elevado apresentaram correlação significativa para disfunção renal ( $p < 0,05$ ). De acordo com a classificação AKIN, o critério fluxo urinário identificou mais disfunção renal do que o critério creatinina. Foi verificado que a disfunção renal ocorreu com maior frequência no 1º pós-operatório e na maioria (82%) dos 63,6% dos pacientes que foram submetidos à cirurgia de revascularização do miocárdio.

**Conclusão:** A maioria dos pacientes (75%) evoluiu inicialmente com disfunção renal sinalizada principalmente pelo critério fluxo urinário da classificação AKIN, número bem superior ao revelado pela creatinina isoladamente. Tal fato confirma que a associação da creatinina sérica com o fluxo urinário tem um desempenho discriminatório superior para a identificação precoce dessa síndrome comparativamente com o rotineiro uso isolado da creatinina.

**Descritores:** Rim/lesões; Marcadores biológicos; Cirurgia cardíaca; Período pós-operatório; Creatinina

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