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CLINICAL RESEARCH

Incidence of acute kidney injury post cardiac surgery: a comparison of the AKIN and KDIGO criteria☆

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Abstract
Background and objectives: Data on urine output have not been routinely presented to define cardiac surgery-related acute kidney injury (AKI). We evaluated the incidence of AKI after cardiac surgery based on the AKIN and KDIGO criteria (considering serum creatinine concentration and urine output in the first 72 hours postoperatively) and compared the performance of the 2 criteria for AKI staging.
Methods: This was a prospective cohort study of adult patients undergoing coronary artery bypass grafting (CABG), valve replacement, or CABG + valve replacement between October 2017 and April 2018 at a single institution. Patients were excluded if baseline creatinine concentration (measured within 7 days before surgery) was $\geq$ 2.5 mg.dL^{-1}. Patients were evaluated for the development of AKI based on changes in urine output and serum creatinine concentration, measured daily from postoperative day 1 to 7, according to the AKIN and KDIGO criteria, which were then compared.
Results: A total of 198 patients were included. AKI occurred in 83.8% by AKIN and in 82.8% by KDIGO, when using both urine output and serum creatinine concentration as defining criteria. Using serum creatinine concentration alone, the incidence of AKI fell to 27.3% by AKIN and to 24.7% by KDIGO. A kappa coefficient of 0.98 was obtained between the AKIN and KDIGO criteria.
Conclusions: Almost perfect agreement was found between AKIN and KDIGO. AKI may be underdiagnosed after cardiac surgery if serum creatinine concentration is used as the only defining criterion. Our findings underscore the fundamental importance of using the urine output criterion in the assessment of patients at risk for AKI.

☆ Study conducted at Instituto de Cardiologia, Fundação Universitária de Cardiologia (IC-FUC), Porto Alegre, RS, Brazil.

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Introduction

Cardiac surgery-related acute kidney injury (AKI) is characterized by deterioration of renal function over a period of hours or days following surgery, and symptoms include oliguria, anuria, paralleling elevations in urea and creatinine concentrations, and development of fluid and electrolyte disorders.[1] As one of the main postoperative complications of cardiovascular surgery, AKI is associated with unfavorable outcomes, such as prolonged hospital and intensive care unit (ICU) length of stay (LOS), increased hospital costs, increased morbidity, progression to chronic kidney disease, need for renal replacement therapy (RRT), hospital readmissions, and in-hospital and long-term mortality.[2–7]

Incidence rates of AKI after cardiac surgery range widely from 8.9 to 39%.[8,9] This wide range may be the result, among other factors, of different criteria used to define AKI, two of which are currently of most use in clinical practice: the Acute Kidney Injury Network (AKIN) criterion and the Kidney Disease Improving Global Outcomes (KDIGO) criterion (Table 1).

Many different definitions of AKI have been suggested by expert working groups, but there is still no clear evidence of the superiority of one classification system over another, despite the tendency to recommend the use of the KDIGO criterion.[10,11] Furthermore, previous studies have not routinely presented data on urine output to define AKI, although this parameter is common to both the AKIN and KDIGO criteria. This practice may be leading to underdiagnosis of AKI, since short periods of oliguria do not correlate with small changes in serum creatinine concentration and may reflect insufficient fluid resuscitation.[12]

The present study was therefore designed to evaluate the incidence of postoperative AKI in patients undergoing cardiac surgery based on two classification criteria, AKIN and KDIGO (taking into account both the serum creatinine concentration and the contribution of the urine output criterion in the first 72 hours postoperatively), and to determine whether there is a difference between the two classification criteria in the staging of AKI. A secondary objective was to evaluate the need for RRT and mortality, both in-hospital and within 30 days of surgery.

Methods

Participants

This was a prospective cohort study of adult patients undergoing elective cardiac surgery with extracorporeal circulation (ECC) from October 2017 to April 2018 at an academic medical center in southern Brazil. The study was conducted in accordance with the provisions of the Declaration of Helsinki and approved by the Institutional Review Board (IRB #2 301 708). Written informed consent was obtained from all participants prior to their inclusion in the study.

All patients aged $\geq$ 18 years admitted during the study period for valve replacement or coronary artery bypass grafting (CABG) with ECC, alone or combined, were included. Exclusion criteria were use of percutaneous procedures (e.g., transcatheter aortic valve implantation), surgery for aortic aneurysm repair or dissection, heart transplant, other cardiac surgeries with ECC, preoperative serum creatinine concentrations $\geq$ 2.5 mg.dL^{-1} regardless of the need for dialysis, need for cardiac reoperation with ECC during the same hospitalization, preoperative serum creatinine concentration measured more than 7 days before surgery, and need for RRT prior to surgery. Patients allocated to another study that had an interventional component in the same institution and those evaluated by other postoperative care teams were not included.

Diagnosis and staging of AKI

Patients eligible for evaluation and follow-up who consented to participate had their personal, clinical, and laboratory data collected preoperatively. Baseline creatinine concentration was measured within 7 days before surgery. After surgery, data were collected daily for 7 consecutive days, including serum creatinine concentration, urine output (first 72 hours), need for RRT, and in-hospital mortality. Urine output was measured during the first 72 hours postoperatively at 6-hours intervals via indwelling urinary catheter while the patient was in the postoperative care unit. The urinary catheter was removed by the nursing team immediately before the patient was discharged from the ICU, as determined by the attending physician.

The day of surgery was defined as day 0. Patients were evaluated for the development of AKI from postoperative day 1 to day 7 based on changes in serum creatinine concentration and urine output according to the AKIN criterion and the KDIGO criterion. The two classification systems were then compared according to each AKI stage. The difference between the two systems lies in the time for the minimum increase in creatinine concentration, i.e., within 48 hours in the AKIN criterion and within 7 days in the KDIGO criterion. As for urine output, the two staging criteria are identical. On postoperative day 30, each patient or next of kin was contacted by telephone for information on survival and need for RRT during the out-of-hospital period. For each patient, at least three attempts at contact were made over a 2- to 4-week period.

Outcomes

The primary outcome was the development of AKI during a 7-day postoperative period, as defined by the AKIN and KDIGO criteria. Secondary outcomes included the need for RRT and all-cause mortality, both in-hospital and within 30 days of surgery.

Statistical analysis

Categorical variables were expressed as absolute and relative frequencies, and continuous variables were expressed as mean and standard deviation (SD). The kappa coefficient was used to assess agreement between the two classification systems (AKIN and KDIGO). Kappa values $\leq$ 0 indicate no agreement, 0.01–0.20 indicate slight agreement, 0.21–0.40 indicate fair agreement, 0.41–0.60 indicate moderate agreement, 0.61–0.80 indicate substantial agreement, and

Table 1 Definition of AKI according to the AKIN and KDIGO criteria.

	AKIN Criterion		KDIGO Criterion	
Stage	**Serum creatinine**	**Urine output**	**Serum creatinine**	**Urine output**
1	Increase in serum creatinine of 1.5 to 2 times baseline level or increase in serum creatinine of ≥ 0.3 mg.dL^{-1} within 48 hours.	Urine output < 0.5 mL.kg^{-1}.h^{-1} for > 6 hours.	Increase in serum creatinine of 1.5 to 1.9 times baseline level within 7 days or increase in serum creatinine of ≥ 0.3 mg.dL^{-1}.	Urine output < 0.5 mL.kg^{-1}.h^{-1} for > 6 hours.
2	Increase in serum creatinine of > 2 to 3 times baseline level within 48 hours.	Urine output < 0.5 mL.kg^{-1}.h^{-1} for > 12 hours.	Increase in serum creatinine of 2 to 2.9 times baseline level within 7 days.	Urine output < 0.5 mL.kg^{-1}.h^{-1} for > 12 hours.
3	Increase in serum creatinine of > 3 times baseline level within 48 hours or increase in serum creatinine to ≥ 4.0 mg.dL^{-1} or initiation of RRT.	Urine output < 0.3 mL.kg^{-1}.h^{-1} for ≥ 24 hours or anuria for ≥ 12 hours.	Increase in serum creatinine of ≥ 3 times baseline level within 7 days or increase in serum creatinine to ≥ 4.0 mg.dL^{-1} or initiation of RRT.	Urine output < 0.3 mL.kg^{-1}.h^{-1} for ≥ 24 hours or anuria for ≥ 12 hours.

AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; KDIGO, Kidney Disease Improving Global Outcomes; RRT, renal replacement therapy.

0.81–1.00 indicate almost perfect agreement.[13] Data were analyzed using SPSS, version 24.0. The level of significance was set at $p < 0.05$ for all analyses.

Sample size was calculated to detect a difference of at least 5% between the incidences of AKI as measured by the AKIN criterion or the KDIGO criterion. This minimum expected difference was obtained from previous studies that have compared the two AKI diagnostic criteria.[8,9,14] Considering a type 1 error rate of 5% and power of 80%, a total of 196 patients would have to be assessed by both AKI diagnostic criteria. Sample size was also calculated for the Cohen's kappa coefficient statistic. We considered a kappa of 0.4 as the upper limit of what would be unacceptably low and a kappa of 0.75 as the lowest value that would indicate substantial agreement. The AKI incidences reported by Fujii et al.[14] of 11.6% for the KDIGO system and 4.8% for the AKIN system were used in the calculation. Considering a type 1 error rate of 1% and power of 90%, a total of 194 patients would have to be assessed by both AKI classification systems to demonstrate substantial agreement (kappa ≥ 0.75) between the two systems under comparison. Iterations of sample size calculations were performed using SPSS, version 21.0, WinPepi, version 11.65, and the R package irr, version 0.84.1.

Results

A total of 198 adult patients undergoing valve replacement or CABG with ECC, alone or combined, from October 2017 to April 2018 were included in the study (Figure 1). Demographic data are shown in Table 2. Most patients were men (57.1%) aged ≥ 60 years (59.6%). CABG alone and valve replacement alone were performed in 48.5% and 45.5% of cases, respectively. The mean (SD) LOS in ICU and duration

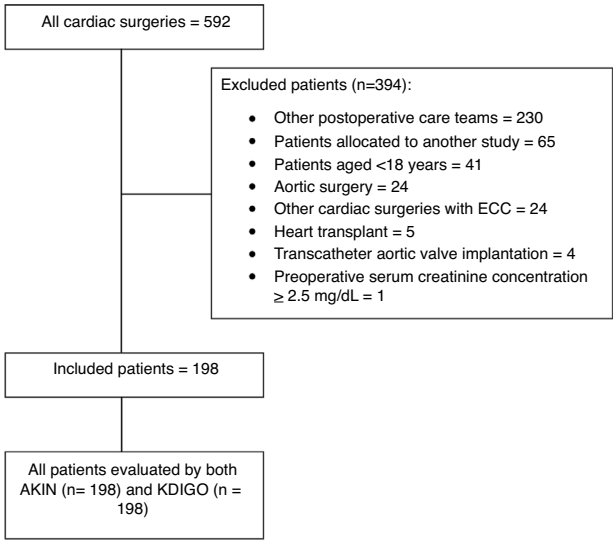

Figure 1 Flow chart of study selection.

of postoperative indwelling urinary catheter use were both 52.3 (14.7) hours (range 36 to 72 hours).

The incidence of any stage AKI according to the AKIN criterion was 83.8% (166/198). If only serum creatinine concentrations were used to define the development of AKI, disregarding urine output, the incidence of patients developing any stage AKI would fall to 27.3% (54/198) (Table 3). According to the KDIGO criterion, 82.8% (164/198) of patients developed AKI. Based on serum creatinine concentration alone, the incidence rate would fall to 24.7% (49/198). When the incidence of AKI was stratified by postoperative day, there was a higher incidence of AKI in the

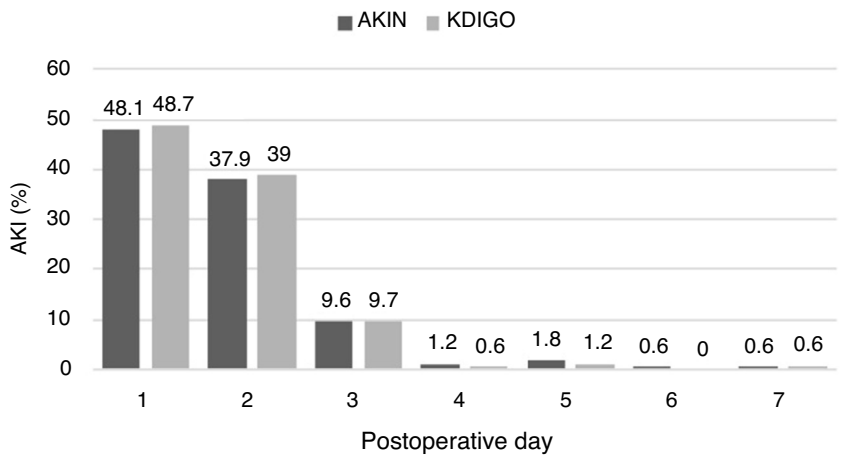

Figure 2 Incidence of AKI per postoperative day.
AKI, acute kidney injury.

Table 2 Characteristics of the study population (n = 198).

Characteristic	n (%) or mean ± SD
Age (years), mean ± SD	61.11 (12.62)
Female, n (%)	85 (42.9)
Weight (kg), mean ± SD	75.5 ± 14.7
Baseline creatinine ($mg.dL^{-1}$), mean ± SD	0.98 ± 0.30
Type of surgery, n (%)	
CABG	96 (48.5)
Valve replacement	90 (45.5)
CABG + valve replacement	12 (6.1)

CABG, coronary artery bypass grafting; SD, standard deviation; n, number of patients.

first 3 postoperative days according to both criteria (Figure 2).

When the evaluations of each patient, as staged according to each classification system, were cross-checked against one another, only 2 patients were classified as AKI stage 1 by the AKIN criterion but as no AKI by the KDIGO criterion (Table 4). The remaining 196 patients were classified equally by the 2 classification systems. The kappa coefficient was 0.98.

Of 198 patients, 2 (1.01%) required RRT during hospitalization, while 3 (1.51%) required RRT during the out-of-hospital period. In all cases, patients received hemodialysis as RRT, accounting for 2.52% of all patients at risk. The rate of all-cause in-hospital mortality was 1.51% (3/198). One patient died intraoperatively, and 2 died on postoperative day 2. The rate of all-cause mortality within 30 days of surgery was 3.31% (6/198). After hospital discharge, 17 (8.58%) patients were lost to follow-up due to inability to contact them for telephone interview.

Discussion

This study prospectively evaluated a significant sample of patients undergoing cardiac surgery and found an incidence rate > 80% of AKI as defined by both the AKIN and KDIGO criteria. There was an almost perfect agreement between the 2 criteria. This was expected considering that most patients were classified as having AKI on the basis of the urine output criterion, which was the same for both AKIN and KDIGO.

The incidence of cardiac surgery-related AKI in our sample was much higher than that reported in previous studies.[6,8,9,15] Both classification systems (AKIN and KDIGO) yielded an incidence rate above 80% due to the use of urine output associated with serum creatinine concentrations as defining criteria. These figures are elevated even in com-

Table 3 Agreement between AKIN and KDIGO classifications of AKI in 198 patients after cardiac surgery – serum creatinine criterion only.

	Stage	KDIGO				Total AKIN (n)
		No AKI	1	2	3	
AKIN	No AKI	144	0	0	0	144
	1	5	42	1	0	48
	2	0	1	1	0	2
	3	0	0	1	3	4
	Total KDIGO (n)	149	43	3	3	198
Kappa coefficient = 0.89 (p < 0.001)						

n, number of patients; AKI, acute kidney injury.

Table 4 Agreement between AKIN and KDIGO classifications of AKI in 198 patients after cardiac surgery – serum creatinine and urine output criteria.

	Stage	KDIGO				Total AKIN (n)
		No AKI	1	2	3	
AKIN	No AKI	32	0	0	0	32
	1	2	46	0	0	48
	2	0	0	101	0	101
	3	0	0	0	17	17
	Total KDIGO (n)	34	46	101	17	198
Kappa coefficient = 0.98 ($p < 0.001$)						

n, number of patients; AKI, acute kidney injury.

parison with AKI in distinct contexts, such as critical care.[16] However, in an analysis based on serum creatinine concentrations alone, this rate falls to 24.7% with KDIGO and to 27.3% with AKIN, producing rates comparable to those reported in the literature. This may be explained by the fact that many previous studies have not assessed urine output immediately after surgery due to several methodological problems, such as difficulty of adequately measuring urine output in the first postoperative days.[17]

The urine output criterion has increased sensitivity to signal changes in renal function compared to serum creatinine concentration.[18] Howitt et al.,[17] in a study involving more than 2,200 patients, showed that patients diagnosed with AKI stage 1 and 2 by creatinine concentration alone or creatinine concentration + urine output, when compared to patients diagnosed by urine output alone, had a higher risk of progression to RRT, of prolonged LOS in ICU and of 2-year mortality (the latter only for creatinine concentration + urine output). They suggested that the KDIGO criterion should be revised due to the increased risk attributed to those patients meeting both creatinine and urine output criteria.[17] Similar findings have been reported by Kellum et al.[19] in a critical care setting, in a study of more than 32,000 patients. Our findings support the above-mentioned data, indicating that this difference can be very significant.

Fujii et al.[14] retrospectively evaluated approximately 50,000 adult patients admitted to a single center and identified AKI by the KDIGO system in 11.6% and by the AKIN system in 4.8%, in both cases using only the serum creatinine criterion. The study included patients admitted to the hospital for multiple reasons.[14] In the present study, the corresponding figures were 82.8% for KDIGO and 83.8% for AKIN. Despite evaluating only patients undergoing cardiac surgery, we obtained a kappa coefficient of 0.98 between the AKIN and KDIGO criteria, which indicates an almost perfect agreement. Besides variations explained by actual differences observed in distinct populations, we believe that the greater agreement between the AKIN and KDIGO criteria in our study may be due to the fact that Fujii et al. have assessed AKI with the creatinine concentration criterion only, without information on urine output, whereas in the present study, both the creatinine variation and urine output criteria were included.

Among patients who developed AKI, most had AKI stage 2. This finding can be attributed to the greater sensitivity of the urine output criterion, since no other relationship was observed when we evaluated the diagnoses made using only creatinine concentration as the defining criterion. Other studies reported a higher incidence of AKI stage 1, followed by AKI stage 2; however, only the serum creatinine criterion was used for diagnosis.[6,9]

According to Petaja et al.,[15] patients diagnosed with AKI by the urine output criterion alone and classified as KDIGO stage 1 had higher mortality up to 2.5 years after surgery than patients without AKI. The worst results were observed in patients who had their diagnosis made within the first 24 hours of surgery. In the present study, most AKI cases occurred during the first 72 hours postoperatively according to both the AKIN and KDIGO criteria. We emphasize the importance of early diagnosis, since there are appropriate interventions to prevent short- and long-term outcomes, such as AKI progression, need for RRT, and mortality.[20,21]

AKI requiring RRT occurs in 2–5% of patients undergoing cardiac surgery and is associated with mortality in up to 60% of cases.[17] AKI is an independent predictor of mortality during the first 5 years after surgery, and more advanced stages are associated with worse short- and mid-term prognosis.[9] In the present study, the rate of RRT was 2.52% and of all-cause mortality was 3% within 30 days of surgery. These rates were lower than expected, as compared with previous studies.[1,2,6,15,22]

This study has some limitations. The number of included patients was limited to the ethically-based minimum necessary to compare the primary outcome ''development of AKI'' as defined by both the AKIN and KDIGO criteria. However, with regard to secondary outcomes, we found low absolute and relative rates for RRT and all-cause mortality within 30 days of surgery. It is possible that we would obtain rates closer to those of previous studies if more patients were included. We did not measure the proportion of patients exposed to diuretics in the postoperative period. No patient received diuretics in the intraoperative period. As shown by a randomized clinical trial, furosemide is responsible for inducing renal dysfunction in the intraoperative and postoperative periods when compared to placebo. That drug is not indicated in the perioperative management of patients submitted to cardiac surgery.[23] Finally, we did not use the RIFLE criterion to assess AKI.

In conclusion, the incidence of postoperative AKI in patients undergoing cardiac surgery based on the AKIN and KDIGO criteria was much higher than expected, highlighting the important contribution of the urine output criterion.

Using the serum creatinine criterion alone may lead to the underdiagnosis of AKI cases. Almost perfect agreement was found between the AKIN and KDIGO criteria for AKI diagnosis and staging. Therefore, both classification systems can be useful in the early identification of patients with AKI following cardiac surgery, thereby helping to improve preventive and therapeutic measures.

Conflict of Interest

The authors declare no conflicts of interest.

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