Original Article

Predictors of Acute Kidney Injury in Critically Ill Patient at Intensive Cardiac Care Unit.

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Abstract

Background: Acute kidney injury (AKI) occurs frequently in the intensive cardiac care unit (ICCU) and is recognized as a heterogeneous syndrome with variable etiology and clinical presentation that affects acute morbidity and mortality. AKI needs to be identified early and underlying causes must be treated.

Methods: We performed a retrospective analysis of the patient registry from Sardjito Cardiovascular Intensive Care (SCIENCE) between January 2021 to December 2021. The KDIGO criteria were used to define AKI characterized by an increase in serum creatinine more or equal to 0.3 mg/dL in 48 hours, or an increase in serum creatinine more or equal to 1.5 times than the previous value, or urine volume less than 0.5 mL/kg BW/hour for 6 hours. Univariate and multivariate data analyses were carried out.

Results: This study included 428 patients with an incidence of AKI was 14,3 %. Univariate analysis showed that AKI was related to diabetes, acute heart failure, sepsis, APACHE II score, SAPS, Sardjito score, MCARS, hemoglobin, leukocyte, and plasma albumin concentration. Furthermore, we did multivariate analysis and showed the independent predictor of AKI at ICCU admission is acute heart failure (OR 3.90; 95% CI 1.95–7.77; p <0.001), sepsis (OR 3.02; 95% CI 1.03-8.90; p 0.045) and high APACHE II score (OR 0.33; 95% CI 0.13-0.80; p 0.015).

Conclusion: Acute heart failure, sepsis, and high APACHE score at admission are independent predictors of AKI among critically ill in ICCU Sardjito General Hospital. The results of this study may contribute to the implementation of targeted therapies.

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Keywords: Acute kidney injury (AKI), Intensive cardiovascular care unit (ICCU).

Introduction

Acute kidney injury (AKI) is recognized as a heterogeneous syndrome that affects acute morbidity, mortality, and a patient's long-term prognosis.[1,2] AKI affects 30–60% of critically ill patients and the overall incidence and prevalence of AKI has increased in recent years.[3] The burden of AKI extends beyond the acute phase with progression to chronic kidney disease (CKD), increased risk of cardiovascular complications, and recurrent episodes of AKI.[4,5] AKI needs to be identified early and underlying causes must be treated or eliminated1. This study aimed to describe the incidence and identify the risk factors of AKI in critically ill patients at the Intensive Cardiac Care Unit (ICCU) at Sardjito General Hospital.

Methods

Study Design

We performed a retrospective observational analysis of the patient registry from Sardjito Cardiovascular Intensive Care (SCIENCE) between January 2021 to December 2021. Study investigators received approval from the Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine, Public Health and Nursing, Gadjah Mada University. Sardjito General Hospital (KE/FK/0228/EC/2021). This registry provided demographic data, risk factors, admission conditions, comorbidities, laboratory and echocardiography findings, several mortality scores, and survival outcomes. Univariate and multivariate data analyses were carried out.

AKI Definition

The KDIGO criteria were used to define AKI characterized by an increase in serum creatinine more or equal to 0.3 mg/dL in 48 hours, or an increase in serum creatinine more or equal to 1.5 times than the previous value, or urine volume less than 0.5 mL/kg BW/hour for 6 hours. Baseline serum creatinine was defined as the serum creatinine value on admission2.

Statistical Analysis

Patients were divided into two groups: patients with and without AKI. Descriptive statistics was conducted using the mean, standard deviation, and frequency values. Categorization was performed for continuous variables, as it is easier to interpret and for the simplicity of reporting results. For common laboratory values, we used the cutoff points which were widely recognized and adopted in clinical practice. The median was used as a cutoff point for several laboratory results. To compare continuous variables between groups with and without AKI, we used the independent Student's t-test. For categorical variables and frequencies, the chi-square test was applied. To explore the risk factors associated with severe AKI, univariable logistic regression models were used. The level of significance was set at 95%. The analysis was performed using the GNU PSPP version 1.4.1-g79ad47, 2019 Free Software Foundation, Inc.).

Results

This study included 428 patients with an incidence of AKI was 14,3 %. In general, the AKI group was older and had more males but with no significant differences. Baseline characteristics of the analyzed study population with complete data are described in **Table 1**.

The patients who developed AKI had a higher prevalence of diabetes (47.5% vs 30.8%; p 0.012), with higher heart rate (94,05 ± 27.92 vs 83,69 ± 25.91; p 0.006). The prevalence of AKI is also increased in patients with acute heart failure (49.2% vs. 16.9%; p <0.001) and sepsis (14.8% vs. 3.3%; p <0.001). Laboratory findings showed patients with AKI tend to have lower hemoglobin levels (11.07 ± 2.45 vs. 12.55 ± 2.43; p <0.001), higher leukocytes (13.76 ± 5.09 vs. 11.81 ± 4.35; p 0.003) and lower albumin levels (3.40 ± 0.65 vs 3.65 ± 0.58; p 0.001). According to several predictive mortality scores at admission (SAPS, APACHE II, Sardjito score, and M-CARS), patients who had AKI had a higher predictive mortality rate than those without AKI.

In bivariate analysis, there were eleven variables associated with AKI i.e., heart rate, diabetes, acute heart failure, sepsis, APACHE II score at admission, SAPS score, Sardjito score, M-CARS score, hemoglobin, leucocyte, and albumin level. The variables with p <

Table 1. Baseline Characteristics (n = 428 patients).

Parameters	AKI (n: 61)	Non-AKI (n: 367)	P value
Sex			0.518
Male	39 (63,9%)	250 (68,1%)	
Female	22 (36.1%)	117 (31,9%)	
Age	62.54 ± 12.09	59.17 ± 13.52	0.068
Risk Factors			
Hypertension	42 (68.9%)	213 (58.0%)	0.111
Diabetes Mellitus	29 (47.5%)	113 (30.8%)	0.012
CKD	2 (3,3%)	10 (2.7%)	0.808
Smoker	30 (49.2%)	191 (52.0%)	0.679
Admission conditions			
Systolic blood pressure	118,5 ± 30,18	121,86 ± 25.57	0.366
Diastolic blood pressure	65,47 ± 13,28	71,50 ± 34,28	0.186
Heart rate	94,05 ± 27.92	83,69 ± 25.91	0.006
Acute heart failure	30 (49,2%)	62 (16.9%)	<0.001
Sepsis	9 (14,8%)	12 (3,3%)	<0.001
Laboratory findings			
Hemoglobin	11.07 ± 2.45	12.55 ± 2.43	<0.001
Albumin	3.40 ± 0.65	3.65 ± 0.58	0.001
Leucocyte	13.76 ± 5.09	11.81 ± 4.35	0.003
Underlying Disease			
Acute coronary syndrome	33 (54.1%)	230 (62.6%)	
Acute heart failure	6 (9.8%)	20 (5.4%)	
Shock	5 (8.2%)	14 (3.8%)	
Vascular disease	4 (6.5%)	37 (10.1%)	
Arrhythmia	8 (13.1%)	41 (11.2%)	
Congenital heart disease	3 (4.9%)	7 (1.9%)	
Miscellaneus	2 (3.3%)	18 (4.9%)	
Echocardiography			
Ejection fraction	44.98 ± 14.20	47.28 ± 13.79	0.170
Tricuspid annular plane excursion	17.54 ± 3.92	18.08 ± 4.49	0.613
Cardiac output	4.15 ± 1.43	4,19 ± 1,27	0.316
Systemic vascular resistance	1443.02 ± 539.02	1664.39 ± 1215.43	0.185
Contrast Use	28 (48,3%)	202 (56,9%)	0.225
SAPS 3 at admission	34.26 ± 14.07	22.78 ± 10.89	<0.001
APACHE II score at admission	15.41 ± 6.98	8.92 ± 5.53	<0.001
Sardjito's score at admission	3.75 ± 2.17	2.00 ± 1.67	<0.001
M-CARS at admission	2.62 ± 1.68	1.27 ± 1.58	<0.001

SAPS = simplified acute physiologic score, APACHE II= acute physiology and chronic health evaluation, M-CARS = Mayo CICU admission risk score, CKD = chronic kidney disease, AKI = acute kidney injury

Table 2. Predictors of AKI obtained by binary multivariate logistic regression analysis (n = 428 patients).

Predictors	OR (95% CI)	P	Adjusted OR (95% CI)	P
Heart rate	1.01 (1.00-1.02)	0.006	0.74 (0.37-1.47)	0.386
Diabetes	2.04 (1.18-3.53)	0.011	1.63 (0.86-3.08)	0.133
Acute heart failure	4.85 (2.73-8.63)	<0.001	3.90 (1.95-7.77)	<0.001
Sepsis	5.12 (2.06-12.74)	<0.001	3.02 (1.03-8.90)	0.045
APACHE II at admission	0.14 (0.07-0.28)	<0.001	0.33 (0.13-0.80)	0.015
SAPS 3 at admission	0.23 (0.13-0.42)	<0.001	0.67 (0.30-1.49)	0.324
Sardjito's Score at admission	0.23 (0.13-0.40)	<0.001	0.85 (0.40-1.82)	0.673
M-CARS at admission	0.23 (0.13-0.41)	<0.001	0.78 (0.37-1.65)	0.515
Hemoglobin	3.26 (1.78-5.98)	<0.001	2.09 (1.00-4.37)	0.051
Leucocyte	0.49 (0.28-0.85)	0.011	0.77 (0.41-1.46)	0.424
Albumin	1.63 (0.94-2.83)	0.084	0.75 (0.37-1.53)	0.427

0.25 found in the bivariate analysis were subsequently included in the multivariate analysis. In multivariate analysis using logistic regression, we found the following factors were significantly associated with AKI at study entry: acute heart failure (Odds Ratio [OR] 3.90; 95% Confidence Interval [CI] 1.95–7.77; p <0.001), sepsis (OR 3.02; 95% CI 1.03-8.90; p 0.045) and high APACHE II score (OR 0.33; 95% CI 0.13-0.80; p 0.015)

Discussion

In this retrospective study of 428 patients admitted to ICCU Sardjito General Hospital, we found that about 14.3% of patients admitted to ICCU developed AKI. This incidence is lower than in studies of AKI in the ICU (25-50%) which may be because patients admitted to the ICCU have a specific clinical spectrum.[6] AKI was associated with high mortality, morbidity, and long-term prognosis regardless of its severity and the association between AKI and poor outcomes persisted in analyses that accounted for different admission diagnoses and clinical characteristics.[4] To prevent further complications, AKI needs to be identified early and underlying causes must be treated or eliminated.[1] In this study, we found the independent predictor of AKI at ICCU admission is acute heart failure, sepsis, and high APACHE II score.

The association between heart failure and renal dysfunction is known as cardiorenal syndrome; while heart failure increases the risk of renal insufficiency and chronic kidney disease, increases the risk of hospitalization and mortality and one type of cardiorenal syndromes is AKI, a syndrome of multiple etiologies associated with increased risk of hospitalization and high mortality.[7] Complex hemodynamics adaptation, neurohumoral dysregulation, and inflammatory and oxidative mechanisms play an important role in the cardiorenal syndrome (CRS).[8] The renin-angiotensin-aldosterone system (RAAS) plays an important role in the progression of kidney damage and worsening of heart failure.[9] The activation of RAAS triggered by a reduced cardiac output and arterial filling pressure, with an elevated central venous pressure (CVP) due to systemic venous congestion and decreased renal perfusion.[10] Furthermore, RAAS activation triggers a pro-inflammatory state associated with destructive oxidative stress and this neurohumoral dysregulation, which are supposed to restore perfusion to vital organs in a compromised circulatory system, can potentially make another detrimental response such as fluid retention, venous congestion, tissue hypoperfusion, inflammation, and oxidative stressors, which can result in progressive deterioration of cardiac and renal function.[11]

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection.[12] Patients with both sepsis and AKI are widely recognized as having an unacceptably high mortality rate.[6] Reportedly, 45–70 % of all AKI is associated with sepsis. 6,13 Several pathophysiological mechanisms that are relatively

specific for sepsis-induced AKI have been proposed but, it should be noted that no single pathway can explain all the features of septic AKI because of the complex process of sepsis and AKI. Sepsis can lead to an inflammatory state and induce another process such as complement and coagulation activation, protease activation (heparan sulfate, elastase), free radical formation, pro-inflammatory cytokine production (IL-1, IL-6, IL-18, TNF-α) and cell activation (neutrophil, macrophage, platelet, endothelial cell). This inflammatory condition can result in direct acute kidney damage. Sepsis can also result in dysregulation of microcirculation that can lead to vasodilation-induced glomerular hypoperfusion and abnormal blood flow within the peritubular capillary network which will worsen kidney damage.[13]

In intensive care scenarios, many prognostic scoring systems, such as the APACHE II, are widely used to predict patient outcomes.[3] A higher APACHE II score had a significant association with the development and severity of AKI in our study. This finding is similar to a previous study that critically ill patients who have a higher APACHE II score are also at a higher risk of AKI.[3,14,15] The risk of hemodynamic derangements associated with worsening severity of illness scores likely is the reason for these findings.[14]

Our study has several limitations. First, our study has a retrospective observational design with its inherent biases and potential for unmeasured confounding variables. Second, this investigation was conducted in a medical intensive cardiac care unit of a tertiary referral center, potentially limiting the generalizability of our study results.

Conclusion

We conclude that acute heart failure, sepsis, and high APACHE score at admission are independent predictors of AKI among critically ill in ICCU Sardjito General Hospital. The results of this study may contribute to the implementation of targeted therapies.

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