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Original Article

Acute Kidney Injury Incidence Following Cardiac Surgery: A Risk Factor Analysis

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Abstract

Background: Acute decline of renal function following cardiac surgery is a common and complex problem with an incidence of up to 30% in Europe and leading to increased mortality rate in immediate and long term. The aim of this study is to analyze risk factors regarding acute kidney injury (AKI) incidence following cardiac surgery. **Patients and Methods:** This was a descriptive cross-sectional study conducted at Dr. Wahidin Sudirohusodo Central General Hospital, Makassar, Indonesia. Serum creatinine level was measured to diagnose AKI. Hemoglobin level, blood transfusion, vasopressor, and inotropic needs before surgery were recorded. Hemodynamic parameters that included mean arterial pressure and heart rate were also recorded. **Results:** Of all 33 subjects who underwent adult cardiac surgery that included coronary artery bypass graft, heart valve, and congenital disease surgery, 21 (63.6%) patients had AKI and 12 (36.4%) patients did not. Several perioperative factor analyses between AKI and non-AKI group revealed that only age showed a significant difference between the two groups ($P = 0.047$). **Conclusion:** Age is the most significant factor in AKI incidence following cardiac surgery. Further studies are required to analyze other perioperative factors that might induce AKI.

Keywords: Acute kidney injury, cardiac surgery, cardiopulmonary bypass

Introduction

Acute decline of renal function following cardiac surgery is a common and complex problem with an incidence of up to 30% in Europe and leading to increased mortality rate in immediate and long term.[1] Data on acute kidney injury (AKI) incidence following cardiac surgery in Indonesia from previous study showed an estimated incidence of 36.4% in pediatric cardiac surgery.[2]

Lewington *et al.* stated that the causes of AKI following cardiac surgery are very complex and multifactorial, including endogenous and exogenous toxins, metabolic factors, ischemic reperfusion, neurohormonal activation, inflammation, and oxidative stress.[3] Distinctive features that occur during cardiac surgery procedure such as cardiopulmonary bypass (CPB) machine and aortic cross-clamp usage, increased blood transfusion volume, and high dose of vasopressor administration will increase AKI incidence following cardiac surgery compared to noncardiac surgery.[1]

The aim of this study is to analyze risk factors regarding AKI incidence following cardiac surgery; therefore, this study might give insight to improve AKI management following cardiac surgery in the future.

Patients and Methods

This descriptive cross-sectional was conducted on October 2019–February 2020 at Dr. Wahidin Sudirohusodo Central General Hospital, Makassar, Indonesia. Population in this study was patients who underwent adult on-pump cardiac surgery. Samples that met inclusion criteria gave their written informed consent. Exclusion criteria in this study were patients with presurgery AKI who underwent hemodialysis, patients with elevated presurgery creatinine level, and patients with a history of kidney transplantation.

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Before this study was conducted, we requested ethical clearance from the Ethical Committee of Biomedical Study on Humans of Medical Faculty of Hasanuddin University and research permit from Dr. Wahidin Sudirohusodo Central General Hospital, where both of them were approved on July 25, 2019, with registration number: 538/UN4.6.4.5.31/PP36/2019. This study is in accordance with Helsinki Declaration 2000. Patients who agreed to join in this study signed their informed consent.

Serum creatinine level was measured 1 day before surgery and once per day for a week postsurgery. Additional measurements were performed based on clinician's advice. Creatinine level postsurgery that was measured for a week was used to diagnose AKI and to determine its grade. AKI based on Kidney Disease Improving Global Outcome (KDIGO) criteria is defined as an elevated absolute creatinine level of 0.3 mg/dl at 48 h or 1.5–1.9 times from baseline level for 7 days. Hemoglobin level, blood transfusion, vasopressor, and inotropic needs before surgery were recorded. Hemodynamic parameters that included mean arterial pressure (MAP) and heart rate were also recorded.

Data of patients' characteristics were presented as frequencies and percentages. Comparison of AKI and non-AKI patients' characteristics was analyzed using Chi-square test. Statistical analysis was performed using SPSS package version 25 for Windows (IBM Corporation, Armonk, NY, USA).

Results

Of all 33 subjects who underwent adult cardiac surgery that included coronary artery bypass graft (CABG), heart valve, and congenital disease surgery, 21 patients (63.6%) had AKI and 12 patients (36.4%) did not.

Table 1 shows the characteristics of cardiac surgery patients. The age of patients varied from 11 to 70 years, with 11–20 years as the group with the lowest percentage and the highest percentage being from group 41–50 years. From 33 samples, 19 were male and 21 were female.

There were several types of cardiac surgery that were conducted: CABG, atrial septal defect closure, mitral valve replacement (MVR), MVR in combination with aortic valve replacement, and ventricular septal defect closure in combination with pulmonary stenosis dilation. Twenty people had heart failure, two people had ejection fraction (EF) <35%, and one person had a previous history of cardiac surgery. Before surgery, one person had intra-aortic balloon pump installation, ten people received chronic obstructive pulmonary disease (COPD) treatment, and five people received insulin.

Table 2 shows on-pump surgery parameter characteristics. CPB was conducted on average for 94.33 ± 30.68 min and cross-clamp was conducted on average for 78.39 ± 30.27 min. The mean blood transfusion volume that was given was 305.74 ± 110.11 ml and the mean hemoglobin level during on-pump procedure was 6.93 ± 1.35 g/dL.

In Table 3, several presurgery factors were analyzed between AKI and non-AKI group, where it was found that age being the only characteristic that had significant difference between AKI incidence (50.57 ± 11.97 vs. 40.50 ± 13.28, $P = 0.047$). Comparison between sex revealed that there were 12 (57.1%) males and 9 (42.9%) females in the AKI group and 7 (58.3%) males and 5 (41.7%) females in the non-AKI group. AKI incidence in CABG procedure was in 16 (76.2%) patients compared to 6 (50%) patients who did not have AKI, and in heart valve surgery, there were 2 (9%) patients who had AKI and 2 (16%) patients who did not. In the AKI group, there were 15 (71.4%) patients with heart failure and 1 (4.8%) patient with EF <35%, whereas in the non-AKI group, there were 5 (41.7%) patients with heart failure and 1 (8.3%) patient with EF <35%.

Table 1: Demographics of the study subjects

Variables	Category	Frequency (n=33), n (%)
Age (years)	11-20	1 (3.0)
	21-30	4 (12.1)
	31-40	2 (6.1)
	41-50	14 (42.4)
	51-60	8 (24.2)
	61-70	4 (12.1)
Sex	Men	19 (57.6)
	Women	14 (42.4)
Surgery type	CABG	22 (66.7)
	ASD closure	6 (18.2)
	MVR	3 (9.1)
	MVR + AVR	1 (3.0)
	VSD closure + PS dilation	1 (3.0)
Heart failure	Yes	20 (60.6)
	No	13 (39.4)
Ejection fraction <35%	Yes	2 (6.1)
	No	31 (93.9)
Cardiac surgery history	Yes	1 (3.0)
	No	32 (97.0)
Presurgery IABP	Yes	1 (3.0)
	No	32 (97.0)
Presurgery COPD therapy	Yes	10 (30.3)
	No	23 (69.7)
Presurgery insulin therapy	Yes	5 (15.2)
	No	28 (84.8)
History of cardiac surgery	CABG	22 (66.7)
	ASD closure	6 (18.2)
	MVR	3 (9.1)

CABG: Coronary artery bypass graft, ASD: Atrial septal defect, MVR: Mitral valve replacement, AVR: Aortic valve replacement, VSD: Ventricular septal defect, PS: Pulmonary stenosis, IABP: Intra-aortic balloon pump, COPD: Chronic obstructive pulmonary disease

Table 2: On-pump parameter characteristics in cardiac surgery patients

On-pump	Mean ± SD	Minimum	Maximum
CPB (min)	94.33±30.68	29.00	165.00
X-clamp (min)	78.39±30.27	16.00	147.00
Transfusion (ml)	305.74±110.11	197.00	559.00
Hb (g %)	6.93±1.35	5.10	10.90

CPB: Cardiopulmonary bypass, Hb: Hemoglobin, SD: Standard deviation

Table 4 shows that there were no significant differences between two groups in terms of on-pump characteristics. The mean CPB and cross-clamp aorta duration in the AKI group were 101.19 ± 23.91 min and 84.67 ± 25.57 min, respectively, whereas in the non-AKI group, the mean durations were 82.33 ± 38.11 min and 67.42 ± 35.63 min, respectively. The mean blood transfusion volume and hemoglobin level in the AKI group were 310.76 ± 105.22 ml and 6.76 ± 1.25 g%, respectively, and in the non-AKI group were 291.50 ± 132.61 ml and 7.25 ± 1.53 g%, respectively.

Discussion

In our study, 21 out of 33 (63%) patients experienced AKI following cardiac surgery. AKI incidence in our study was higher than several studies.[1,4-6] Differences in diagnostic techniques in determining AKI could be one of the reasons for different AKI incidences from each study. We used KDIGO criteria in determining AKI diagnosis in our study, using both creatinine and urine production criteria. The use of risk/injury/failure/loss/end-stage (RIFLE) and AKI network (AKIN) criteria following cardiac surgery without correcting changes in serum creatinine due to fluid balance will make AKI diagnosis less detectable. KDIGO criteria is associated with higher sensitivity in diagnosing AKI and predicting mortality compared to RIFLE and AKIN. KDIGO criteria, which is a combination of AKIN and RIFLE classifications, is commonly used for AKI diagnosis following cardiac surgery.[7-12]

Table 3: Comparison of characteristics between acute kidney injury and nonacute kidney injury group

Variables	AKI incidence		*P**
	Yes (*n*=21)	No (*n*=12)	
Age (years)	50.57±11.97	40.50±13.28	0.047
Sex			
Male	12 (57.1)	7 (58.3)	1.000
Female	9 (42.9)	5 (41.7)	
CABG surgery	16 (76.2)	6 (50.0)	0.149
Heart failure	15 (71.4)	5 (41.7)	0.142
Ejection fraction <35%	1 (4.8)	1 (8.3)	1.000
History of previous cardiac surgery	1 (4.8)	0	1.000
History of DM	5 (23.8)	1 (8.3)	0.379
History of hypertension	20 (95.2)	10 (83.3)	0.538
IABP presurgery	1 (4.8)	0	1.000
COPD treatment presurgery	5 (23.8)	5 (41.7)	0.433
Insulin presurgery	4 (19.0)	1 (8.3)	0.630
ACE-inhibitor presurgery	13 (61.9)	3 (25)	0.071
Valve surgery	2 (9%)	2 (16%)	0.610
Dobutamine intra-surgery	3.1±4.9	1.4±2	0.449
Norepinephrine intra-surgery	0.08±0.08	0.06±0.07	0.699

*Chi-square test. AKI: Acute kidney injury, CABG: Coronary artery bypass graft, DM: Diabetes mellitus, IABP: Intra-aortic balloon pump, COPD: Chronic obstructive pulmonary disease, ACE: Angiotensin converting enzyme

Table 4: Procedure duration and laboratory results during on-pump procedure in cardiac surgery patients

Variable	AKI incidence		*P**
	Yes (*n*=21)	No (*n*=12)	
CPB (min)	101.19±23.91	82.33±38.11	0.100
X-clamp (min)	84.67±25.57	67.42±35.63	0.123
Transfusion volume (ml)	310.76±105.22	291.50±132.61	0.708
Hb (g %)	6.76±1.25	7.25±1.53	0.326

*Chi-square test. AKI: Acute kidney injury, CPB: Cardiopulmonary bypass, Hb: Hemoglobin

Several perioperative factor analyses between AKI and non-AKI group revealed that only age showed a significant difference between the two groups ($P = 0.047$). Factors behind elderly to more likely develop AKI might be due to decreased kidney function, patient's comorbidities, or related medical treatment received by elderly patients. Decreased renal mass due to reduced weight and decreased of glomeruli volume and number are morphological and anatomical factor due to renal age.[13-17]

This study is in accordance with a study conducted by Guan *et al*., which stated that age is one of the factors associated with AKI incidence following cardiac surgery.[18] Age factor varied widely in several other studies as a risk for AKI following cardiac surgery.[18-21] Jiang *et al*. showed that although the numbers differed, they did not show a statistically significant difference.[19]

The use of angiotensin-converting enzyme (ACE) inhibitor and hypertension history are risk factors for AKI incidence following cardiac surgery. In this study, the use of ACE inhibitor did not show significant differences between AKI (13 patients = 61.9%) and non-AKI group (three patients = 25%). The use of ACE inhibitor as a risk factor has been studied by several experts. Arora *et al*. carried out a cohort study of 1358 patients and found an increased risk of AKI by 27.6%.[22] This is in accordance with other studies conducted by Kristovic *et al*., which showed an association between ACE inhibitor use and AKI incidence following cardiac surgery and Whiting *et al*. who conducted a meta-analysis study of perioperative ACE inhibitor use.[23,24]

In our study, there was no significant difference for comorbid hypertension between AKI (20 patients = 95.2%) and non-AKI (ten patients = 83.3%) group. Hypertension is one of the AKI predictors following cardiac surgery. This is largely due to renal vascular damage due to chronic hypertension and a shift in autoregulation exacerbated by CPB use with low-pressure MAP condition.[25]

There was no significant difference for diabetes mellitus (DM) comorbid between AKI (five patients = 23.8%) versus non-AKI (one patient = 8.3%) group. This is in accordance with the studies reported by Ferreiro and Lombardi and Kanji *et al*.[20,25] Several studies have shown that DM is a risk factor for AKI following cardiac surgery. This is due to diabetic nephropathy

which will cause damage to tubules and glomerulus.[26] Insulin-dependent DM is a strong risk factor in AKI incidence following cardiac surgery, which was not in accordance with this study. Arun *et al*. also reported that 80% of DM patients suffered from AKI compared to 20% of non-DM patients who underwent CABG surgery.[27]

Patients with low EF (<35%) in our study did not differ significantly between AKI and non-AKI group. Low EF is a risk factor because it reduces perfusion to kidneys. Pieri *et al*. stated that low EF increases AKI risk following cardiac surgery. This was more prominent in patients with EF <35%.[28] Omar *et al*. in their study found that patients with lower EF suffered from AKI more compared to non-AKI patients.[29]

Our study also did not show a significant difference for COPD comorbid between AKI (five patients = 23.8%) versus non-AKI (five patients = 41.7%). The mechanism of COPD effect on AKI incidence of AKI is still unclear. This is probably because of a decrease in arterial oxygen content which affects oxygen delivery to kidney tissue. Several studies have shown the effect of COPD risk factors on AKI incidence following cardiac surgery, although the results are not significant.[19,30]

In this study, the mean CPB and cross-clamp durations in AKI cases were 101.19 ± 23.91 min and 84.67 ± 25.57 min, respectively, while in the non-AKI group, the durations were 82.33 ± 38.11 min and 67.42 ± 35.63 min, respectively. CPB and aortic cross-clamp duration were associated with AKI incidence following cardiac surgery. This is due to elevated inflammatory factors and ischemic reperfusion injury.[31] In their study, Sirvinskas *et al*. demonstrated that AKI incidence following cardiac surgery was significant if CPB duration was around 134 min and aortic cross-clamp duration was 75 min.[32] Karim *et al*. showed that the risk of AKI increased with CPB duration >70 min and aortic cross-clamp duration >60 min.[33]

Of all AKI patients, 16 (76.2%) underwent CABG surgical procedures compared to 6 (50%) patients in the non-AKI group. Two (9%) AKI patients underwent heart valve surgery compared to 2 (16%) patients in the non-AKI group. There was no significant differences between the two groups in terms of CABG or valve surgery. Valve surgery is a complex procedure, with prolonged surgery that might cause hemodynamic instability in renal perfusion. Ramos and Dias reported that valve replacement surgery was a strong predictor of AKI incidence following cardiac surgery (odds ratio [OR] = 4.7, $P = 0.002$; 95% confidence interval [CI] = 1.76–12.62).[34]

In this study, PRC transfusion volume and Hb levels were 310.76 ± 105.22 ml and 6.76 ± 1.25 g%, respectively, in the AKI group, and 291.50 ± 132.61 ml and 7.25 ± 1.53 g%, respectively, in the non-AKI group. Although it is not statistically significant, transfusion volume that was given was larger in the AKI group and Hb level in AKI patients was lower compared to non-AKI patients. Intraoperative blood transfusion might increase oxygen delivery, but also increase AKI risk following cardiac surgery. This is because red blood cell transfusion will cause an increase of free heme due to hemolysis process in stored blood, therefore damaging the kidneys. Crosina *et al*. reported that intraoperative hematocrit level was a factor that increased AKI incidence's area under curve that was combined with Cleveland clinical score, with hematopoietic cell transplantation = 0.25 ± 0.03 versus 0.28 ± 0.04 ($P = 0.001$) and transfusion volume = 1.51 ± 2.13 versus 0.6 ± 1.44 ($P = 0.001$).[35] A research conducted by Baranauskas *et al*. showed that anemia incidence was around 7.59%, and there was a significant positive correlation between perioperative anemia and AKI ($r = 0.50, P < 0.05$).[36] Ng *et al*. found that low hematocrit levels and preoperative anemia were potential modifiable risk factors associated with AKI following cardiac surgery in the Asian population, whereas administration of blood transfusions did not affect AKI incidence.[37]

Inotropes and vasopressors use (dobutamine and norepinephrine) did not show significant differences between AKI (dobutamine = 3.1 ± 4.9 mcg/kg/min), (norepinephrine = 0.08 ± 0.08 mcg/kg/min) and non-AKI (dobutamine = 1.4 ± 2 mcg/kg/min), (norepinephrine = 0.06 ± 0.07 mcg/kg/min). The use of inotropes and vasopressors is associated with postsurgery AKI incidence due to renal ischemia and reperfusion due to hemodynamic instability and decreased cardiac function. Ramos and Dias found that norepinephrine (OR = 3.32, $P = 0.013$; 95% CI = 1.29–8.58) and dobutamine (OR = 5.3, $P = 0.019$, 95% CI = 1,32–21,64) were predictors of AKI incidence following cardiac surgery.[34]

This study had limited number of samples (33 patients). Furthermore, other perioperative factors that induce AKI following cardiac surgery should be analyzed in future studies.

Conclusion

Age is the most significant factor in AKI incidence following cardiac surgery. Further studies are required to analyze other perioperative factors that might induce AKI.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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