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Original Article

ACUTE KIDNEY INJURY FOLLOWING CORONARY ARTERY BYPASS GRAFTING WITH CARDIOPULMONARY BYPASS AT DR. SOETOMO GENERAL ACADEMIC HOSPITAL SURABAYA: A PRELIMINARY STUDY

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ABSTRACT

Introduction: Acute Kidney Injury (AKI) is a significant cause of morbidity and mortality following common cardiac surgery. The most common cardiac surgery performed at Dr Soetomo General Academic Hospital Surabaya is coronary artery bypass grafting (CABG). Along with the increasing number of these procedures performed on subjects, Cardiopulmonary Bypass (CPB) has also grown in popularity, which is frequently associated with postoperative AKI. **Objective:** To investigate the incidence of postoperative AKI in subjects who had undergone a CABG procedure using the CPB technique. **Materials and Methods:** A retrospective study was conducted at Dr. Soetomo General Academic Hospital in Surabaya. All subjects who had CABG with CPB in 2019 were included in the study. The incidence of AKI was determined by comparing the creatinine serum level before and after surgery on days 0, 1, 2, 3, and >3 according to the AKIN criteria. **Results and Discussion:** The 68 subjects who underwent the CABG with CPB procedure were made up of 53 males (77.9%) and 15 females (22.1%). The average age of the subjects was 58.209.07. This study included 63 subjects (five subjects could not be evaluated due to incomplete data), and AKI was diagnosed in 44 of them using the AKIN criteria (69.8%). Postoperative AKI was reported in 14 subjects (22.2%) on day 0, 18 subjects (28.6%) on day 1 post-operation, and the same number of 6 subjects (9.5%) on day 2 and day 3 post-operation. None of them had AKI after the third post-operative day. **Conclusion:** More than 50 % of cases of post-CABG Acute Kidney Injury (AKI) occur at Dr. Soetomo General Academic Hospital, with the majority occurring on the first day after surgery.

Keywords: Acute Kidney Injury; CABG; Cardiovascular Disease; CPB; Postoperative Cardiac Surgery

ABSTRAK

Pendahuluan: Seiring dengan peningkatan *Coronary Artery Bypass Grafting* (CABG), teknik *Cardiopulmonary Bypass* (CPB) juga lebih sering digunakan. Tindakan ini adalah operasi jantung yang paling umum dilakukan di RSUD Akademik Dr. Soetomo Surabaya. Hal ini sering menyebabkan *Acute Kidney Injury* (AKI) pascaoperasi. Beberapa kondisi terkait dengan kejadian AKI pasca CPB. **Tujuan:** Untuk mengetahui kejadian AKI pascaoperasi pada pasien yang telah dilakukan CABG dengan teknik CPB. **Bahan dan Metode:** Penelitian ini merupakan penelitian deskriptif retrospektif di RSUD Dr. Soetomo Surabaya. Semua pasien yang menjalani CABG dengan CPB pada tahun 2019 diteliti. Kejadian AKI dievaluasi dengan membandingkan kadar kreatinin serum sebelum dan sesudah operasi pada hari ke 0, 1, 2, 3, >3 menggunakan kriteria AKIN. **Hasil dan Pembahasan:**Ada 68 pasien yang menjalani teknik CPB, 53 pasien (77,9%) berjenis kelamin laki-laki dan 15 pasien (22,1%) berjenis kelamin perempuan. Usia rata-rata pasien adalah 58,20 ± 9,07. Diantaranya, 44 pasien (69,8%) dari 63 memenuhi kriteria AKI berdasarkan kriteria AKIN. Lima pasien tidak dapat dievaluasi karena data yang tidak lengkap. Empat belas pasien (22,2%) mengalami AKI pascaoperasi pada hari ke 0, 18 (28,6%) pada hari 1 pascaoperasi, dan 6 pasien (9,5%) didiagnosis AKI pada hari ke 2 dan ke 3 pascaoperasi. **Kesimpulan:** Angka kejadian AKI pasca CABG dengan CPB di RSUD Dr. Soetomo lebih dari separuh dari total kasus yang dikerjakan, dan sebagian besar terjadi pada hari pertama pascaoperasi.

Kata kunci: *Acute Kidney Injury*; CABG, Penyakit Kardiovaskular; CPB; Pascaoperasi Bedah Jantung

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INTRODUCTION

Coronary Artery Bypass Grafting (CABG) is a procedure that replaces an occluded coronary artery with arteries or veins from other parts of the patient's body in order to restore normal blood flow (1). This is the most common type of thoracic and cardiovascular surgery in the world (2). There was no national data on the epidemiology of the procedure in Indonesia. The total number of CABG procedures performed in Dr. Soetomo General Academic Hospital Surabaya in 2018 and 2019 is 82 and 68, respectively.

Cardiopulmonary bypass (CPB) is a surgical technique in which a machine temporarily replaces the heart and lung function, maintaining blood circulation and oxygen levels; thus, heart surgery can be performed (3). This technique may contribute to the occurrence of AKI due to the systemic inflammatory response, disruptions in regional blood flow, renal vasomotor tonus, and microemboli formation (3). AKI can be caused by kidney diseases (such as acute interstitial nephritis, acute glomerulosclerosis, and vasculitis kidney disease) as well as abnormalities outside the kidney (such as prerenal azotemia and postrenal obstructive nephropathy). AKI can also be caused by acute lung failure or an acute coronary syndrome. All of these conditions may contribute to direct kidney injury, which can lead to kidney failure (1).

To characterize and analyze AKI, the majority of the studies employed the Acute Kidney Injury Network (AKIN) standards. These measurements are based on serum creatine levels or an adjustment of serum creatinine (expanded by roughly 1.5 times the benchmark) and pee yield (0.5 ml/kg/h for approximately 6 hours). The limitation of these standards is their use without revision for serum creatinine changes inferable from liquid equilibrium during a liquid revival at CPB technique, which leads to underdiagnosis of AKI (4). The advantage of using these criteria is that AKI is calculated without the need for urine output, and AKIN only encompasses three days of hospitalization.

Table 1. AKI criteria based on AKIN (2).

AKI degree	Urine production	AKIN
1	<0.5 mL/kg/hours in 6-12 hours	Creatinine serum 1.5-2x baseline level or an increase ≥0.3 mg/dL for 48 hours
2	<0.5 mL/kg/hours in >12 hours	Creatinine serum >2-3x baseline level
3	<0.3 mL/kg/hours in >24 hours or anuria for >12 hours	Creatinine serum >3.0x baseline level or an increase >4.0 or RRT

Silva et al. conducted a forthcoming accomplice investigation on adult subjects who underwent CABG. When serum creatinine fixation and pee yield were both used, AKI occurred in 83.3 % of the 198 subjects. By AKIN using serum creatinine concentration alone, the frequency of AKI was 27.3 %. The use of pee yield to analyze AKI from AKIN measures was significant (3). According to other studies, the incidence rate of AKI after heart surgery was 49 % (81.63 % class I AKIN) on day 2 post-surgery based on

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AKIN criteria (2). According to Amini et al., 15.8% of subjects developed AKI (275 out of 1737 subjects). Subjects with AKI had a longer ventilation time, ICU stay, and medical clinic stay (P 0.001). Death rates in subjects with and without AKI were 28 (10.2%) and 22 (1.5%), respectively (P 0.001) (4).

CPB with >70 minutes and cross-clamp time >60 minutes increase the risk of AKI after heart surgery by OR of 4.76 and 2.84, respectively (p0<05) (5). On day 60, the mortality rate after severe AKI with the need for renal transplantation was 52.6 %, and on day 90, it was 44.7 %. Another findings revealed that the mortality rate on day 30 in AKI patients who required renal transplantation after heart surgery was 58.6 % (6). CABG was performed on approximately 22-57 % of all hospitalized subjects suffering from AKI (7).

The following conditions were associated with an increased risk of post-CPB AKI: 1) Old age and female sex; 2) pre-operative heart disease; 3) emergency surgery; 4) peripheral arterial disease; 5) repeated intervention; 6) insulin-dependent diabetes; 7) intraoperative aprotinin use; 8) chronic obstructive pulmonary disease (COPD); and 9) pre-operative renal disfunction (6,8,9).

Cho et al. revealed that 23.9 % of subjects had AKI despite having a normal preoperative renal capacity. Indeed, even with early recovery of renal capacity within 3 days, AKI increased the risk of Acute Kidney Disease (AKD) (OR 3.21, 95 % CI 1.98–5.20, P0.001) and Chronic Kidney Disease (CKD) (OR 2.86, 95 % CI 1.68–4.86, P0.001), while persistent AKI increased the risk of AKD (OR 12.07, 95 % CI 5.56–26.21, P0.001) and CKD (OR 10.54, 95 A multivariable analysis identified CPB is needed as a preventive approach to reduce the number of the incidence of AKI. 3-month postoperative cardiovascular breakdown and high right ventricular systolic pressing factor as free risk factors for CKD (10). Preoperative renal function is a risk factor for postoperative AKI. Preoperative kidney work has an impact on outcomes because impaired renal capacity prior to a medical procedure leads to more regrettable consequences such as a longer length of hospitalization and a higher mortality rate (11).

From 2000 to 2010, the number of mortalities caused by cardiovascular methods increased by 28%. Up to half of the subjects who underwent heart medical procedures with CPB are predisposed to severe kidney injury. Cardiac Surgery-Associated Acute Kidney Injury (CSA-AKI) patients who require Renal Replacement Therapy (RRT) have a death rate of up to 60%. The frequency is increasing in conjunction with the heinous death rate. This increased the length of medical clinic stay as well as other long-term outcomes such as persistent kidney disease, death rate, and emergency clinic costs. As a result, it is critical for an early conclusion to direct procedures to protect renal capacity (12).

The CPB technique has become more popular as the number of CABG procedures performed in subjects has increased. The number of CABG surgeries in Indonesia is expected to rise in the coming years due to improvements in hospital facilities and an increase in the number of cardiothoracic surgeons. Dr. Soetomo General Academic Hospital Surabaya has performed heart surgeries since 1960, and the number of procedures has continued to rise to the present day (13). Therefore, identification of risk factors causing AKI following

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This study was aimed to investigate the incidence of postoperative AKI in subjects who underwent CABG with CPB.

MATERIALS AND METHODS

This was a retrospective descriptive study performed at Dr. Soetomo General Academic Hospital Surabaya. The study included all subjects who had a CABG with CPB technique performed during surgery at Dr. Soetomo General Academic Hospital Surabaya in 2019. All subjects who had CABG with CPB technique at Dr. Soetomo General Academic Hospital Surabaya met the inclusion criteria. All data, such as CPB duration and creatinine level before and after surgery, were obtained from a medical record. Subjects with incomplete data in their medical records were excluded. The incidence of AKI was assessed using the AKIN criteria. The Research Ethics Committee of Airlangga University's Faculty of Medicine approved this preliminary study. Each patient's personal information was kept private and was only used for research purposes.

The incidence of AKI was determined by comparing creatinine serum levels before and after surgery on days 0, 1, 2, 3, and >3, according to AKIN criteria. Meanwhile, the Cockcroft-Gault formula was used to calculate eGFR (14).

$$CrCl\left(\frac{mL}{minute}\right) = \frac{(140 - age)x\ \text{body weight (kg)}}{Creatinine\ serum\ \left(\frac{mg}{dl}\right) x\ 72}\ (x0.85\ in\ female)$$

Tables were used to display the univariate data. The numeric data was shown in minimum and maximum values and mean ± deviation standard. The categorical data were presented in the form of a frequency and percentage (%).

RESULTS AND DISCUSSION

At Dr. Soetomo General Academic Hospital Surabaya, 68 patients underwent CPB surgery. Males made up 77.9% of the 53 subjects, while females made up 15%. (22.1 percent). The diagnosis of subjects who underwent CPB surgery varied, but the majority were diagnosed with CAD-TVD (45 subjects: 66.2 %) (Figure 1). According to the patient distribution, the mean age was 58.2 ±9.07, with the youngest being 30 years old and the oldest being 83 years old. The shortest CPB session lasted 61 minutes, while the longest lasted 243 minutes. Preoperative creatinine serum levels ranged between 0.6 and 2.4747. The postoperative creatinine serum level was 0.59 at the lowest and 6.0 at the highest (Table 2).

According to the findings of this study, the shortest CPB duration among 65 subjects was 61 minutes, while the longest was 243 minutes. The average duration was 123.98±38.16. According to the data, the average duration of CPB was 123 minutes, increasing the risk of postoperative AKI. The duration of CPB was one of the risk factors for postoperative AKI. A CPB duration of more than 8 hours increases the risk of AKI by fourfold (8,15). A longer time in CPB may result in hemostatic disorders, increasing transfusions and limiting oxygen transport, which will stimulate inflammation mediators, causing kidney disruption (16,17). Several studies found that a prolonged cumulative CPB period (>180 minutes) was associated with a higher mortality rate, postoperative complications, intensive care unit length of stay, and length of mechanical ventilation. As a result, the recommended CPB/grafting time and cumulative CPB time should be less than 56 minutes and 180 minutes, respectively, to avoid the aforementioned side effects (18).

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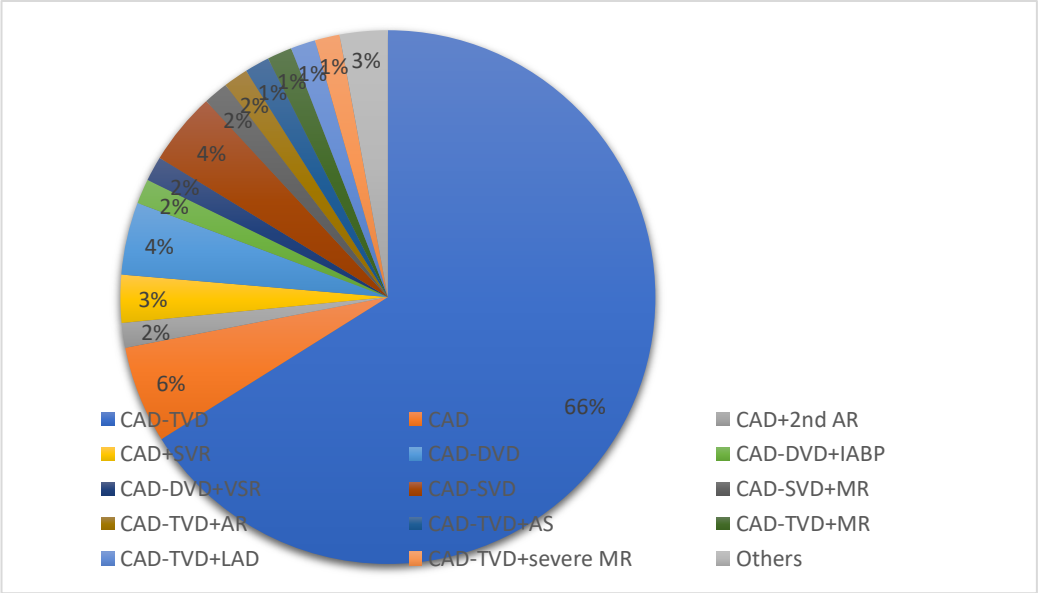

Figure 1. Frequency of surgery with CPB technique based on the diagnosis

Five of the 68 subjects who met the inclusion criteria had incomplete data, so they were unable to be evaluated for this study. AKI was diagnosed in 38 of the 63 subjects studied (60.3 %) based on AKIN criteria, which is more than the number of subjects who were not diagnosed with AKI (19 subjects, 39.7%). The incidence of AKI after heart surgery was assessed on postoperative days 0, 1, 2, and 3. Out of 44 subjects with AKI, 14 (22.2%) were diagnosed on postoperative day 0, 18 (28.6%) on postoperative day 1, 6 (9.5%) on postoperative day 2, 6 (9.5%) on postoperative day 3, and none were diagnosed after postoperative day 3 (Table 3).

Acute kidney injury (AKI) is characterized by a rapid decrease in kidney function over a period of hours to days. AKI was identified by an increase in creatinine serum and blood urea nitrogen (BUN) levels, as well as a decrease in urine production (19). AKI was classified using an increase in creatinine serum and urine production based on AKIN criteria (14). The mechanism of AKI development in CPB was connected to a decrease in renal perfusion (low flow hypoperfusion, low pressure no pulsatile perfusion) caused by vasoconstriction. The vasoconstriction was caused by the activation of free radicals, complement, inflammation mediators, decreased cardiac output (hypotension), and RAAS (2).

Hemodilution and hypothermia resulted in low pressure and no pulsatile perfusion. The inflammatory response can keep afferent arteriole constriction going. Long-term hypotension can lead to renal compensation exhaustion, filtration reserve exhaustion, and endogenous and/or exogenous vasopressors increasing afferent arteriole resistance, resulting in decreased GFR. Oliguria may occur at this stage of prerenal azotemia; however, tubular function may still be intact. A longer ischemic period will result in tubular structure injury and cell disruption, preventing tubular with back leak into circulation. The phenomenon of oxidative injury and inflammation causes further hypoperfusion and damage in tubular cells (20).

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Table 2. Description of the characteristic of the patient and the risk factors

Variable	N	Minimum	Maximum	Mean±SD
Age	55	30	83	58.20±9.07
Bodyweight	63	39	90	66.48±11.85
Body height	63	143	176	161.86±6.32
CPB duration	65	61	243	123.98±38.16
Creatinine serum				
Preoperative	60	0.60	2.47	1.21±0.38
Postoperative D0	58	0.59	2.87	1.30±0.46
Postoperative D1	30	0.75	4.94	2.05±0.91
Postoperative D2	24	0.85	5.95	2.27±1.21
Postoperative D3	23	1	5	2.71±1.24
Postoperative D>3	21	1	6	2.33±1.39
eGFR				
Preoperative	55	20	201	73.58±32.09
Postoperative D0	53	15	252	70.15±38.41
Postoperative D1	29	7	94	47.86±21.27
Postoperative D2	23	6	149	44.91±30.28
Postoperative D3	21	9	61	35.76±13.82
Postoperative D>3	19	11	153	46.00±35.17

Notes:
D0: early postoperative
D1: postoperative day 1
D2: postoperative day 2
D3: postoperative day 3
D>3: postoperative after day 3
CPB: Cardiopulmonary Bypass

In this study, eGFR was found to decrease from post-surgery until the third day of surgery, after which it began to rise (Preop 73.58±32.09, 70.15±38.41, 47.86±21.27, 44.91±30.28, 35.76±13.82, 46.0±035.17). The Cockcroft-Gault formula was used to calculate the estimated glomerular filtrtration rate (eGFR). This formula used body weight to calculate creatinine clearance in mL/minute (21). Alteration in eGFR is connected to creatinine clearance from collected urine after 24 hours and Gentamycin clearance (22,23). A multicenter prospective study found that the Cockcroft-Gault formula could be used to predict the prognosis of a cardiovascular event, specifically mortality and bleeding (24). Nevertheless, in a diabetic patient, GFR calculated using the Cockcroft-Gault formula was overestimated (25).

Table 3. Description of the incidence of AKI

Variable	n (%)
Total AKI diagnosis (n = 63)	
AKI	44 (69.8)
No AKI	19 (30.2)
Postoperative AKI (n = 44)	
AKI D0	14 (22.2)
AKI D1	18 (28.6)
AKI D2	6 (9.5)
AKI D3	6 (9.5)
AKI D>3	0 (0)

Notes:
AKI: acute kidney injury (An increase of creatinine serum ≥0.3 or > 1.5 times baseline value / preoperative)
D0: early postoperative
D1: postoperative day 1
D2: postoperative day 2
D3: postoperative day 3
D>3: postoperative after day 3

Glomerular filtration rate (GFR) was an important factor in determining AKI incidence in post-cardiac surgery subjects. Preoperative eGFR is a risk factor for postoperative AKI, and subjects with a preoperative eGFR of 70 mL/min/1.73m^2 have a higher incidence of AKI (26). Meta-analysis study on eGFR value before CPB operation showed a correlation between low eGFR value with AKI where preoperative GFR of <30 mL/min/1.73m^2 was a risk factor of postoperative AKI and increases the risk of AKI for more than 4,000 times (8,15,26,27).

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This study has limitations, such as other risk factors for AKI after 48 hours that were not investigated; thus, we cannot conclude the etiology of AKI caused by perioperative-CABG on ICU subjects with elevated creatinine serum on postoperative day 3.

CONCLUSION

The majority of AKI situations were encountered on the first postoperative day. After postoperative day 3, there was no evidence of AKI. More studies with more complete parameters (creatinine serum and urine production) or using biomarkers for kidney injury, as well as analysis of other factors causing AKI and patient outcomes, are required so that we can gain a better understanding of AKI after CABG.

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