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PREOPERATIF SERUM URIC ACID LEVELS PREDICT ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY

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Abstract

Background: Cardiac surgery has been associated with impaired renal parenchymal function precisely in the tubular system. This causes Acute Kidney Injury (AKI), which started from the operation and persisted to postoperative in various time span. This decrease in kidney function leads to the accumulation of residual plasma products, such as urea and creatinine. Concentrations of uric acid may be associated with kidney disease without intrarenal uric acid crystal deposition. Additionally, hyperuricemia associated directly with hypertension, metabolic syndrome, chronic kidney disease, and peripheral vascular disease. Moreover, hyperuricemia is a common finding in patients with coronary vascular disease. Thus, preoperative hyperuricemia may be linked to an increased risk of AKI after CABG. This study aims to determine the level of preoperative uric acid serum can predict the incidence of Cardiac Surgery-Associated AKI (CSA-AKI) at the Haji Adam Malik General Hospital.

Methods: This retrospective cohort study of 100 patients underwent coronary artery bypass graft (CABG) at the Haji Adam Malik General Hospital from January 2019 to December 2019. All patients will be examined for preoperative and postoperative laboratory. For serum uric acid values will be divided into 2 groups, namely group 1, namely patients with serum uric acid levels <6.5 μg / dL (normal), and group 2 with serum uric acid levels> 6.5 μg/dL (Hyperuricemia). Then the patient will be followed during hospitalization. Then conducted analysis to see association between serum uric acid level and incidence of CSA-AKI.

Results: The highest incidence of postoperative coronary artery surgeries occurred in the serum level of uric acid in group 2 compared to group 1. In group 2 the incidence of postoperative AKI was 39 people (59.1%) while in group 1 there were 9 people (25.6%) with a P-value of 0.002. Multivariate analysis showed that uric acid >6.5 μg/dL was the most dominant risk factor affecting the incidence of postoperative AKI [OR 3.69 (1.19-11.43), p = 0.023].

Conclusion: A high serum uric acid level (> 6.5 μg/dL) is a strong predictor of the incidence of postoperative AKI in coronary artery bypass surgery with an OR of 3.69.

Introduction

Heart surgery has been linked to malfunctioning of various organ systems, one of which is damage to the kidneys. Damage to the kidneys occurs in the kidney parenchyma precisely in the tubular system. This results in Acute Kidney Injury (AKI), which starts from the operation process and lasts postoperatively in various time frames. [1]

The term AKI is used to describe the rapid decline (hours to days) of kidney function. This decline in kidney function causes the accumulation of residual plasma products, such as urea and creatinine. The definition of AKI has changed and evolved over the years, making comparisons of events and prevalence between studies difficult. An estimated 2-18% of patients treated in hospitals have AKI. [2]

The incidence of AKI as a postoperative complication of the heart often occurs. The average incidence of postoperative AKI of the heart ranges from 7.7 to 40% depending on the patient population and acute kidney injury significantly increases the risk of death. Patients who develop a postoperative AKI often require dialysis, which results in increased ICU length of stay and increased long-term morbidity. Mild kidney functions postoperative cardiac surgery that does not require dialysis are also significantly associated with poor clinical outcomes. [3]

The existence of gout as a marker of cardiovascular disease has been known since 1897 by Dr. Davis. Due to the absence of good epidemiological studies, this uric acid level was ignored until the 1960s. Since then many epidemiological studies have linked high uric acid levels to several cardiovascular conditions such as hypertension, metabolic syndrome, coronary heart disease, cerebrovascular disease, vascular dementia, preeclampsia, and kidney disease.

The pattern of elevated uric acid levels was studied in 316 subjects with coronary heart disease who suffer from acute coronary syndrome found a pattern of uric acid levels that increased in the first week during an acute attack of coronary heart disease and decreased gradually until the third month after a heart attack, this was mainly found in male patients than in women. [4]

Methods

This study was an observational study with a retrospective cohort design and a single center to prove preoperative serum uric acid levels as a predictor of AKI post-cardiac surgery. Inclusion criteria were all patients who underwent CABG surgery who did not receive allopurinol therapy before heart surgery, had no history of hemodialysis or peritoneal dialysis before heart surgery, did not have chronic kidney disease. Exclusion criteria were incomplete data or no previous uric acid examination, a serum creatinine increase 1.5 times from the baseline that was previously known or assumed to have occurred within 7 days. The value of serum creatinine > 1.5 mg / dL. Patients who will undergo cardiac surgery are grouped into 2 groups namely group 1 are patients who are said to have normal uric acid, while group 2 is patients who are said to suffer from hyperuricemia when the serum uric acid level is more than 6.5 mg/dl. The main outcome assessed was the incidence of AKI after cardiac surgery.

Patient data is filled in sheets containing clinical and laboratory data. Clinical data consists of age, sex, comorbidity, and type of surgery. Laboratory tests are carried out before and after heart surgery at the hospital. Blood tests were carried out in the Adam Malik Hospital Pathology Clinical laboratory. For preoperative laboratory data were taken within 7 days before surgery and postoperative laboratory taken within 48 hours after surgery. When more than one creatinine laboratory result was found within 48 hours postoperatively, the highest serum creatinine was taken as postoperative data. Data is collected by researchers and then analyzed.

Categorical variables are presented with the number or frequency (n) and percentage (%). Numerical variables are assigned mean values and standard deviations for normally distributed data, while non-distributed numerical data use a median (middle value), which is then compared with student t-test or Mann Whitney U test. Normality test in variables numerically all subjects used one sample of Kolmogorov Smirnov (n> 50) or Shapiro Wilk (n <50). For samples found to be significant in the bivariate analysis test, the next step is the multivariate test. Statistical data analysis using statistical software, p <0.05 was considered statistically significant.

Result

The total number of research subjects was 100 people, consisting of 91 men and 9 women. The results of this study found research subjects with 48 AKI and 52 non-AKI people. The average age of study subjects with a 58-year-old AKI compared to 57 years in non-AKI subjects. There were 45 men who had postoperative AKI of the heart and 46 people who did not experience postoperative AKI. In table 1, the average Body Mass Index (BMI) in the two groups also did not differ statistically with a value of 25.6 kg / m2 at AKI and 25.4 kg / m2 at non-AKI. From the laboratory examination also found no statistically significant differences between groups with AKI and non-AKI postoperative groups from the results of Hb examination, blood sugar levels when, HbA1c, preoperative heart. The AKI group had Hb levels with an average of the non-AKI group of 13.8 g / dL compared to 14 g / dL. The average preoperative blood sugar level was 209 mg / dL in the AKI group and 235 mg / dL in the non-AKI group. The average preoperative HbA1c value was 6.3% in the AKI group and 6.6% in the non-AKI group.

Found a statistically significant difference in risk factors for the incidence of AKI between the AKI and non-AKI groups where hypertension was 40 people in the AKI group and 39 people in the non-AKI group (p = 0.036). Whereas in DM 33 people in the AKI group and 41 people in the non-AKI group did not find any statistically significant differences.

The results of this study indicate that there are statistically significant differences between the AKI and non-AKI groups in terms of preoperative laboratory examinations. The mean preoperative creatinine value was 1.47 mg / dL in the AKI group and 0.88 mg / dL in the non-AKI group (p <0.001). The mean value of preoperative uric acid was 8.4 mg / dL in the AKI group and 6.8 mg / dL in the non-AKI group (p = 0.002). The mean GFR in the AKI group was lower at 53 mL/min / 1.73 m2 while in the non-AKI group it was higher with a value of 92.5

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mL/min / 1.73 m2 (p <0.001). The average value of total cholesterol was 155 mg / dL and in the non-AKI group it was 166 mg / dL (p = 0.098). The mean value of intraoperative Cardiopulmonary bypass time in the AKI group was higher at 45 (53.6%) while in the non-AKI group it was lower by 39 (46.4%) (p = 0.011). The mean value of intraoperative Off-pump surgery in the AKI group was lower at 3 (18.8%) while in the non-AKI group it was higher with a value of 13 (82%) (p <0.001).
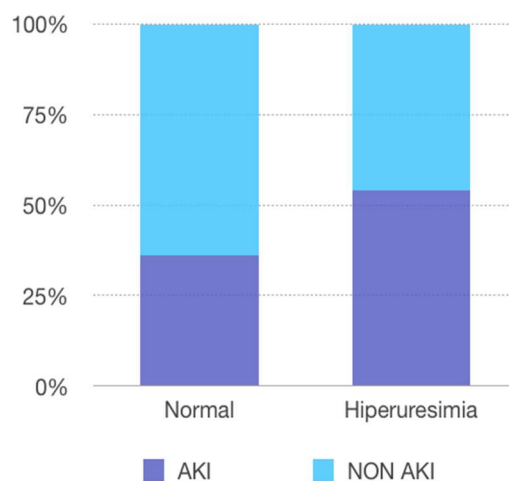
Table 1. Data characteristics of research subjects

Variables	AKI (n= 48)	Non AKI (n= 52)	P Value
Age (years)	57±6,1	56±5,3	0,595[c]
Gender (%)	Male 45 (93,8)	Male 46 (88,5)	0,356 [a]
	Female 3 (6,3)	Female 6 (11,5)	
BMI (kg/m^2)	25,6±4,38	25,4±3,72	0,833[c]
DM (%)	33(44,6%)	41 (78,8%)	0,250[b]
Hypertension (%)	40(83,3%)	39(75%)	0,036[a]
Hb (g/dL)	14,0±28,8	13,8±1,54	0,970 [c]
HbA1C (%)	6,3±1,5	6,6±1,98	0,626 [c]
Glucose ad random (mg/dL)	209±95	235±87,9	0,300 [c]
Creatinine (mg/dL)	1,47(0,67-1,49)	0,88(0,36-1,40)	<0,001[c]
Uric Acid (mg/dL)	8,4 (4,8-15,2)	6,5 (4,17-6.8)	0,002[c]
GFR (mL/min/1,73 m^2)	53±26,2	92,5±37,5	<0,001[c]
Cholesterol Total	155±31,9	166±34,5	0,098 [c]
Cardiopulonary bypass time < 100 (min)	45(53,6%)	39 (46,4%)	0,011[a]
Off-pump surgery	3 (18,8%)	13 (82%)	0,011[a]

　　　To assess the effect of serum uric acid values on the incidence of CSA-AKI, the patients were divided into 2 groups based on preoperative serum uric acid levels, group 1 ie patients with serum uric acid levels <6.5 mg / dL (normal) with the number of patients 9 people, and group 2 with serum uric acid levels > 6.5 mg / dL (hyperuricemia) with 39 patients.

　　　From this study, a significant difference was found between patients with normal serum uric acid levels with hyperuricemia for CSA-AKI. The results showed that the highest CSA-AKI incidence occurred in the serum level of uric acid in group 2 compared to group 1. In group 2 the incidence of CSA-AKI were 39 people (59.1%) while in group 1 there were 9 people (26, 5%) with a P-value of 0.002 (figure 1).

Table 2. Comparison of AKI after cardiac surgery based on serum uric acid levels

Variables	Normal (<6,5 µg/dL) (n=35)	Hyperuricemia (>6,5 mg/dL) (n=64)	P Value
AKI (%)	9 (26,5%)	39 (59,1%)	0,002 [a]

*Figure 1. Comparison graph of AKI based on cardiac surgery
serum uric acid level*

After obtaining a description of the data characteristics of research subjects who experienced AKI and non-AKI postoperative heart, performed a bivariate analysis to determine the variables that can be included in the multivariate analysis. Bivariate analysis was performed using logistic regression methods with a significance level of p <0.05.

Based on the results of the logistic regression bivariate analysis it was found that serum levels of uric acid, hypertension, CBP time, GFR values increase the risk of postoperative AKI of the heart. Whereas age, sex, hemoglobin, and type 2 DM are not related to CSA-AKI events are described in table 3.

Serum uric acid level > 6.5 mg / dL (group 2) is associated with an increased incidence of postoperative AKI [OR 0.25 (0.10-0.62), p = 0.002]. The complete bivariate analysis of data is presented in table 4.

Table 3. Bivariate analysis of several variables for AKI after cardiac surgery

Variables AKI	OR	95% CI		P Value
		Min	Max	
Uric Acid	0,25	0,10	0,62	0,002
Age ≥ 60 years	0,55	0,23	1,32	0,174
Gender (male)	0,52	0,12	2,17	0,356
Hypertension	2,40	1,04	5,56	0,038
DM	1,70	0,69	4,20	0.250
Cardiopulonary bypass time < 100 (min)	0,20	0,06	0,76	0,011
HB <13 g/dL	1,54	0,62	3,82	0,355
GFR (mL/min/1,73 m^2)	32,2	7,0	147,5	<0,001

Multivariate analysis was performed after obtaining the results of a bivariate analysis using logistic regression tests and a value of p <0.05 was considered significant. Variables included in multivariate analysis were variables obtained from univariate analysis with p values <0.25 (table 4).

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Multivariate analysis in this study is useful to find out which independent variables are the most dominant and affect the incidence of CSA-AKI. From a multivariate analysis, it was shown that only 2 independent factors could predict the occurrence of CSA-AKI, namely serum gout with serum uric acid level> 6.5 mg / dL and Cardiopulmonary bypass time intraoperative. Uric acid serum> 6.5 mg / dL is a risk factor that affects an increase in the incidence of postoperative AKI of the heart [OR 3.69 (1.19-11.43), p = 0.023].

Table 4. Multivariate analysis of several variables for AKI after cardiac surgery

Variables AKI	OR	95% CI		P Value
		Min	Max	
Uric Acid	3,69	1,19	11,4	0,023
Cardiopulonary bypass time	20,3	1,93	211,2	0,012
GFR (mL/min/1,73 m^2)	0,01	0,01	0,13	<0,001

Discussion

Subjects in this study were collected consecutively, patients who underwent CABG surgery from January to December 2019. In this study data were taken from medical records of heart surgery patients from January to July 2019 and August to December 2019 from the current status of patients hospitalized for heart surgery. The total sample in this study was 100 patients who met the inclusion criteria and did not meet the exclusions.

Constraints encountered when collecting samples in the form of incomplete laboratory data, especially on samples taken from medical records, so that some patient data cannot be included in the study sample.

The implementation of research is in accordance with the ethical principles of medical research in using humans, so in determining research procedures it is necessary to consider human dignity and the benefits and disadvantages of a study. For this reason, this study was approved by the ethics committee of the Faculty of Medicine, University of North Sumatra.

As for obtaining a postoperative AKI, the heart is carried out through observations starting from before the surgery until the day the patient goes home for outpatient treatment.

From 100 research subjects, it was found that there were 91 male sexes with an average age of 50 years. This shows the difference in the average age of the younger 9-10 years compared to the average age obtained from research Joung et al (2014) which is 63 years. This study also found research subjects with hypertension of 40 people (83.3%) and type 2 DM 33 people (44.6%).

This study shows that serum levels of uric acid that are higher than normal preoperatively are associated with decreased kidney function and worse outcomes in postoperative heart surgery patients.

CSA-AKI is a common complication of heart surgery. From previous studies showing ± 30% of people who undergo heart surgery will experience CSA-AKI. The incidence of AKI as a postoperative complication of the heart often occurs. According to RIFLE and AKIN criteria, the range of CSA-AKI events between 9-39% depends on the clinical profile of the patients analyzed, and the type of heart surgery. [5]

The average CSA-AKI incidence ranges from 7.7 to 40% depending on the patient population and acute kidney injury significantly increases the risk of death. In this study the incidence of CSA-AKI was 59.1% with a higher incidence of postoperative CABG AKI compared to the rate of heart valve surgery. This is the same as research conducted by Joung et al (2014) which shows a higher incidence of postoperative CABG AKI at high serum uric acid levels, which is around 53%.

Research conducted by Joung showed that serum uric acid levels> 6.5 μg / dL was associated with a 53% increase in kidney disease progression compared to normal serum uric acid levels <6.5 μg / dL, around 39%. The study also showed that high serum uric acid levels were associated with higher CSA-AKI events. Where in this study found the incidence of CSA-AKI at high uric acid levels> 6.5 μg / dL which is 59.1%, normal uric acid level <6.5 μg / dL 26.5%. This allows that high levels of uric acid will affect clinical outcomes worse than normal serum uric acid levels. [6]

In this study the bivariate analysis showed high serum uric acid levels (> 6.5 μg / dL), hypertension, cardiopulmonary bypass time and intra-operative off-pump surgery had significant values as risk factors for

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increased CSA-AKI events. However, after multivariate analysis, only 2 independent factors can predict the occurrence of postoperative AKI, namely high serum uric acid levels (> 6.5 µg / dL) and Cardiopulmonary bypass time with the most dominant risk factors influencing the incidence of CSA-AKI is a high serum uric acid level > 6.5 mg / dL [OR 3.69 (1.19-11.43), p = 0.023]. This is in line with Lee's research, preoperative high serum uric acid levels are predictors of CSA-AKI events. [7,8]

The exact mechanism underlying the relationship of high serum uric acid concentrations with the incidence of postoperative AKI of the heart remains unclear. However, there are several possibilities, Hyperuresemia which is characterized by an increase in serum uric acid concentrations known to interfere with autoregulation of blood flow to the kidneys through renal vasoconstriction caused by activation of the renin-angiotensin-aldosterone system and inhibition of renal nitric oxide synthase neurons. Gout has also been shown to induce proinflammatory activity and oxidative stress, causing injury to the renal tubulointerstitial, thereby causing a decrease in kidney function. [9,10]

Conclusion

High serum uric acid levels (> 6.5 mg / dL) are associated with the incidence of postoperative AKI compared to normal serum uric acid levels (<6.5 mg / dL). High serum uric acid level or hyperuricemia (> 6.5 mg / dL) is one predictor of the incidence of postoperative AKI of the heart with an OR of 3.69.

Conflict of Interest

The authors declare that there is no conflict of interest.

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