Jurnal
Kardiologi Indonesia
J Kardiol Indones. 2013;34:147-53
ISSN 0126/3773

Clinical Research

Risk of Acute Renal Failure Requiring Renal Replacement Therapy after Cardiac Surgery

Juweni Joe, Zuswahyuda Samsu, April Retno, Rita Zahara, Ronggo Prakoso, Ardiyan

Background: Acute renal failure is a rare but serious complication following cardiac surgery and associated with increased mortality and morbidity.
Objective: To identify factors associated with mortality and mortality of patients with acute renal failure after cardiac surgery treated with continuous renal replacement therapy.
Method: This was a cohort retrospective study on cardiac surgery patients who developed acute renal failure requiring renal replacement therapy after surgery in Harapan Kita National Cardiac Center between January 2011 and April 2012. Data was retrieved from medical record and consisted of pre-operative, intra-operative, and post-operative variables. Risk factor identification was done using multivariate logistic regression analysis, whereas relative risk analysis was applied to know the association between risk factor and morbidity. Direct or indirect effect of variables on renal failure was analyzed using Barttlet's and anti-image correlation test.
Results: A total of 110 cases were obtained during the study period; 70 (63.3%) among them were men. Patients mean age was 57.6 years. Pre-operative renal failure, New York Heart Association Functional Classification Class (NYHA) class IV, critical condition, coronary revascularization surgery and bleeding, post-operative anemia, bleeding and venous saturation <65% showed a trend of mortality and morbidity rate between 0.1 and 9.1. The Keiser-Meyer-Olkin (KMO) value and Barttlet's test showed that re-surgery, bleeding and low inotropic score resulted in 31.63% probability of having post-operative renal failure.
Conclusion: Re-surgery, bleeding and inotropic use may result in post-operative renal failure.

Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Indonesia and National Cardiovascular Center Harapan Kita, Jakarta

(J Kardiol Indones. 2013;34:147-53)

Keywords: factor analysis, renal failure, continuous renal replacement therapy, cardiac surgery

Jurnal
Kardiologi Indonesia
J Kardiol Indones. 2013;34:147-53
ISSN 0126/3773

Penelitian Klinis

Risiko Gagal Ginjal Akut Pasca Bedah Jantung yang memerlukan Terapi Pengganti Ginjal Kontinyu

Juweni Joe, Zuswahyuda Samsu, April Retno, Rita Zahara, Ronggo Prakoso, Ardiyan

Latar belakang: Gagal ginjal akut merupakan komplikasi serius pasca bedah jantung yang jarang terjadi tetapi terkait dengan peningkatan kemungkinan terjadinya mortalitas dan morbiditas.
Tujuan: Untuk mengetahui faktor-faktor risiko yang berhubungan mortalitas dan morbiditas pasien gagal ginjal akut dengan terapi pengganti ginjal kontinu pasca bedah jantung.
Metode: Penelitian ini adalah studi kohort retrospektif pada pasien pasca bedah jantung yang mengalami gagal ginjal akut dengan terapi pengganti ginjal kontinyu di Pusat Jantung Nasional Harapan Kita antara Januari 2011 dan April 2012. Data diambil dari rekam medis yang meliputi riwayat medis pra-operasi, data intra-operasi dan pascaoperasi. Identifikasi faktor risiko mortalitas dilakukan dengan analisis multivariat logistik regresi, sedangkan analisis risiko relatif dilakukan untuk mengetahui hubungan faktor risiko dan morbiditas. Besaran pengaruh variabel yang secara langsung atau tidak langsung mempengaruhi gagal ginjal dianalisis dengan uji Barttletdan *anti-image correlation*.
Hasil: Sebanyak 110 kasus dikumpulkan selama periode penelitian; 70 (63,3%) di antaranya adalah laki-laki. Rerata usia pasien adalah 57.6 tahun. Gagal ginjal, gagal jantung *New York Heart Association Functional Classification Class* (NYHA) kelas IV, kondisi kritis pra-operasi, revaskularisasi koroner dan perdarahan, anemia, perdarahan, dan nilai saturasi vena kurang dari 65% pascaoperasi menghasilkan kecenderungan rasio mortalitas dan morbiditas antara 0,1 sampai 9,1. Nilai Keiser-Meyer-Olkin (KMO) dan hasil uji Barttlet menunjukkan bahwa re-operasi, perdarahan dan inotropik skor yang rendah memberikan kemungkinan 31,63% gagal ginjal pasca-operasi.
Kesimpulan: Re-operasi, perdarahan dan penggunaan inotropik dapat menyebabkan gagal ginjal pascaoperasi bedah jantung.

(J Kardiol Indones. 2013;34:147-53)

Kata kunci: analisis faktor, gagal ginjal, terapi pengganti ginjal kontinu, pasca bedah jantung

Background

Renal failure requiring continuous renal replacement therapy after cardiac surgery increases hospital cost, morbidity and mortality.[1] The risk of renal failure after cardiac surgery is 4% and most of the patients would need dialysis therapy afterwards.[2,3] Risk factors identification in patients with high risk of renal failure after cardiac surgery has been studied using the European System for Cardiac Operative Risk Evaluation (Euro SCORE). However, it may not be strong enough to predict mortality rate in high risk patients and combined surgery. Risk

Alamat Korespondensi
Dr. Juweni Joe, SpGk, ICU BedahJantung, PusatJantungNasional-Harapan Kita. Jl. Jendral S. ParmanKav. 54, Slipi, Jakarta
E-mail: *weni.1202@yahoo.com*

factor identification is important to manage patients optimally before surgery and to reduce morbidity and mortality. Therefore, this study was aimed to evaluate the relationship among risk factors (pre-, intra- and post-operatively) and mortality of acute renal failure requiring continuous renal replacement therapy after cardiac surgery.

Method

Study design and subjects

This was a retrospective cohort study in the Intensive Care Unit, Harapan Kita National Cardiac Center. Subjects were patients underwent cardiac surgery between January 2011 and April 2012 who developed renal failure requiring continuous renal replacement therapy. Inclusion criteria were patients underwent coronary revascularization procedure, valve repair or valve replacement and combined coronary revascularization or valve repair. Patients with congenital anomaly were excluded.

Risk factors categories and assessment

Risk factors for mortality due to renal failure requiring continuous renal replacement therapy were categorized as pre-operative, intra-operative, and post-operative variables. Pre-operative risk factors were body mass index (BMI), prior history of cardiac surgery, type 2 diabetes on insulin treatment, emergency surgery, type of surgery, left main disease, severe renal dysfunction, severe pulmonary hypertension, ejection fraction, and NYHA Class IV heart failure. Body mass index was defined as body weight in kilogram divided by body height in meter square (kg/m^2). The results were grouped as underweight (BMI <18.5 kg/m^2), normal (BMI 18.5-22,9 kg/m^2), overweight (BMI 23-25 kg/m^2), or obese (BMI >25 kg/m^2). Pre-operative critical conditions were ventricle fibrillation, ventricular tachycardia, cardiac and pulmonary resuscitation, mechanical ventilation, inotropic treatment or intraaortic balloon pump (IABP), anuric acute renal failure or urine production less than 10 mL/ hour. Emergency surgery was defined as an immediate surgery after a diagnostic procedure. Pre-operative renal failure was established if the creatinine clearance was more than 50 mL/ minute. Severe pulmonary hypertension was defined as increased pulmonary arterial pressure more than 55 mmHg. Left ventricle function was categorized based on the left ventricular ejection fraction [LVEF] as follows: good (LVEF >50%), moderate (LVEF 31-50%), poor (LVEF 21-30%), and very poor (LVEF <20%). NYHA class IV heart failure was established if the patient was not able to perform light activity.

Intra-operative risk factor was the cardiac bypass time of more than 90 minutes. Post-operative risk factors consisted of re-surgery, bleeding, anemia, inotropic score, and venous oxygen saturation. Re-surgery was a repeated surgery within 24 hours. Bleeding was defined as a blood loss of more than 2.5 liter within the first 24 hours. Anemia was established if there was a reduction of hemoglobin (Hb) level to more than 50% of the pre-operative value.[4] Venous oxygen saturation reflects the venous blood saturation on average, which returns to the right side of the heart from all tissues. Body tissues usually utilize only 25% of the available oxygen, while the rest 75% is reserved for increasing activity or physiologic stress.[5] Inotropic score was calculated as dopamine in µg/kg/min x 1+ milrinoneµg/kg/min x 15 + epinephrine in µg/kg/min x100. Inotropic score were grouped as low (<20), moderate (21-30) and severe (>30).[6]

Data analyses

Sampling adequacy was tested using the Kaiser-Meyer-Olkin (KMO) – Barttlet's test and anti-image correlation. Sample is adequate if the KMO and anti-image correlation values were greater than 0.5. Major component analysis was applied to measure the effects of variables on data variance. Effect of variables on mortality was tested using the multivariate logistic regression analysis with Hosmer and Lemeshow test (HLT) (α= 15% and 95% confidence interval). The HLT was chosen because it is more sensitive than the omnibus value. The HLT value is consistent with Chi-square distribution: the low HLT value, the nearer Chi-square distribution. Assessment of the effect of variables on morbidity was done using the relative risk analysis. Due to sample limitation, relative risk was manually calculated from morbidity on independent variables. Data analysis was done using the statistical software SPSS version 15.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Characteristics of the study subjects

There were 1520 patients underwent cardiac surgery between January 2011 and March 2012. Renal failure was present in 110 patients and were treated with continous renal replacement therapy. Patients' mean age was 57.6 years. Seventy (63.6%) of the patients were men. Most patients underwent coronary revascularization procedure **(Table 1).** There were 46.4% of patients who overweight. Mean pre-operative LVEF was 49.1%. There were 90 (81.8%) patients with pre-operative renal dysfunction with a mean creatinine clearance of 54.1 mL/minutes.

Mortality rate was 40.9% and most cases occurred in patients underwent coronary revascularization. Mortality was 11.8% in patients with more than one cardiac surgery procedures. Lowest mortality rate was found in patients underwent off-pump coronary revascularization. The mean ICU stay was 12.3 days whereas the mean hospital stay was 30.8 days **(Table 2)**.

Table 1. Characteristics of the study subjects (N=110)

Characteristic	Mean (SD)	N	%
Age (years)	57.6 (12.8)		
Age ≥70 years		13	11.8
Gender			
• Male		70	63.6
• Female		40	36.4
Body mass index			
• Less than normal		15	13.6
• Normal		32	28.1
• Overweight		51	46.4
• Obese		12	10.9
Medical history			
• Previous cardiac surgery		6	5.5
• Hypertension		33	30.0
• Diabetes on insulin treatment		10	9.1
• Previous neurological dysfunction		7	6.4
• Pre-operative renal dysfunction		99	90.0
• Pre-operative dialysis		8	7.3
Mean ejection fraction of left ventricle	49.1 (17.1)		
Ejection fraction of left ventricle <30%		23	20.9
Type of surgery			
• Coronary revascularization		52	47.3
• Other		58	52.7
IABP		24	21.8
Emergency surgery		10	9.1

Table 2. Post-operative variables and the outcomes (N=110)

Variable and outcomes	Mean (SD)	N	%
Inotropic use after surgery			
• Epinephrine		26	23.3
• Dobutamine		85	77.3
• Milrinone		36	7.2
Severe bleeding		28	25.5
Post-operative parameters			
• Mean arterial pressure (mmHg)	75.7 (15.9)		
• Mean venous oxygen saturation (%)	71.4 (12.7)		
• Hemoglobin <7 mg/ dL		10	9.1
Outcomes			
• Died		45	40.9
• Mean ICU stay (days)	12.3 (13.9)		
• Mean hospital stay (days)	30.8 (23.4)		

Sampling adequacy and principal component analysis

The value of KMO test was 0.621 which indicate that the sample was adequate for further analysis. Removal of variables, which had anti-image values less than 0.5, resulted in increased KMO value to 0.640 ($p<0.001$).

Table 3. Multivariate analyses of all risk factors to predict post-operative mortality.

Variable	Odds ratio (95% confidence interval)	p value
Preoperative factors		
Previous surgery	0.88 (0.09 – 8.22)	0.925
Pre-operative critical condition	7.10 (2.30 – 2.91)	0.004
Diabetes on insulin treatment	0.90 (0.20 – 4.15)	0.913
Emergency surgery	7.10 (2.30 – 2.91)	0.258
Coronary revascularization	0.90 (0.20 – 4.15)	0.136
Left main disease	1.14 (0.40 – 3.22)	0.837
Renal dysfunction	0,61 (0.34 – 1.07)	0.150
Left ventricle dysfunction	0.69 (0.41 – 1.19)	0.267
Heart failure NYHA class IV	1.99 (1.05 – 3.79)	0.075
Severe pulmonary hypertension	0.97 (0.63 – 1.51)	0.916
Intra-operative factor		
Cardiac bypass time >90 minutes	0.66 (0.23 – 1.93)	0.525
Post-operative factors		
Low inotropic score	0.19 (0.09 – 0.64)	0.022
Re-operation	0.35 (0.09 – 1.26)	0.177
Severe bleeding	2.96 (0.99 – 8.94)	0.102
Post-operative anemia	9.12 (0.89 – 92.93)	0.117
Venous saturation <65%	0.39 (0.16 – 0.98)	0.093

Table 4. Multivariate analysis adjusted from post-operative mortality (α= 0.15)

Variable	Odds ratio (95% confidence interval)	*p* value
Male sex		0.314
Female sex		1.000
Normal BMI		0.100
Overweight or obese		0.676
Age ≥50 years		1.000
Pre-operative factors		
• Prior surgery	0.20 (0.01 – 3.09)	0.332
• Pre-operative critical condition	3.39 (1.09 – 10.57)	0.076
• Diabetes on insulin treatment	0.77 (0.14 – 4.29)	0.806
• Emergency surgery	0.42 (0.07 – 2.43)	0.413
Coronary revascularization		
• Left main disease	1.58 (0.54 – 4.50)	0.481
• Renal dysfunction	0.41 (0.19 – 0.91)	0.067
• Left ventricle dysfunction	0.56 (0.32 – 0.98)	0.090
• NYHA class IV heart failure	2.00 (0.98 – 4.08)	0.109
• Severe pulmonary hypertension		0.107
Intra-operative factor		
• Cardiac bypass time >90 minutes	0.58 (0.19 – 1.72)	0.406
Post-operative factors		
• Low inotropic score	0.30 (0.06 – 1.55)	0.227
• Re-surgery	0.59 (0.13 – 2.69)	0.569
• Severe bleeding	0.55 (0.15 – 2.05)	0.456
• Post-operative anemia	1.57 (0.90 – 2.00)	0.999
• Venous saturation >65%	0.57 (0.20 – 1.58)	0.365

Factor extraction by principal component analysis was then applied with the following results:

- First principal component comprised of *re-surgery within 48 hours, bleeding and inotropic score;*
- Second principal component comprised of *age* and *hypertension;*
- Third principal component comprised of *type of surgery*, *cardiac bypass time>90 minutes,* and *renal dysfunction;*
- Fourth principal component comprised of *diabetes* and *emergency surgery;*
- Fifth principal component comprised of *anemia*, *bodymass index*, and *pre-operative critical condition*.

Each of the principal components could explain about 31.6%, 21.9%, 17.6%, 15.3%, and 13.6% of the variance, respectively. These results showed that the first component (re-surgery, bleeding, and inotropic score) can explain 31.6% of the variance within the data.

Multivariate logistic regression analysis

There was no difference among gender, BMI and age less than 50 years. This condition was contradictory in patients aged more than 50 years with pre-operative critical condition which increased the probability of mortality by 7.1 times higher than patients without pre-operative critical condition.

In general, pre-operative critical condition, renal failure, NYHA class IV heart failure, coronary revascularization procedure, anemia and post-operative bleeding, and venous saturation >65% were identified as factors which increased mortality rate.

Patients with bleeding after cardiac surgery had 92 times increased risk of death compared to patients with no bleeding. Factors which did not show effect on mortality rate were diabetes on insulin treatment, LVEF <30%, severe pulmonary hypertension, emergency surgery, cardiac bypass time of more than 90 minutes, and re-surgery. By using a level of significance at 95% on relative risk predictor of post-operative morbidity from pre-operative, intra-operative and post-operative variables, only pre-operative condition had significant effect on mortality rate **(Table 5)**.

Table 5. Predictors of morbidity after surgery

Variable	Relative Risk (95% confidence interval)
Pre-operative factors	
• Prior surgery	0.72 (0.41 – 1.28)
• Pre-operative critical condition	1.13 (1.05 – 1.23)
• Diabetes on insulin treatment	1.11 (1.04 – 1.19)
• Emergency surgery	1.11 (1.04 – 1.19)
• Left main disease	0.99 (0.86 – 1.13)
Intra-operative factor	
• Cardiac bypass time >90 minutes	0.93 (0.88 – 1.03)
Post-operative factors	
• Re-surgery	0.90 (0.73 – 1.12)
• Severe bleeding	0.88 (0.73 – 1.05)
• Post-operative anemia	0.82 (0.73 – 1.12)
• Venous saturation <65%	0.82 (0.46 – 1.45)

Discussion

Previous study showed that the incidence of renal failure after cardiac surgery may increase if there were several risk factors present, such as pre-operative

renal dysfunction, diabetes, low LVEF, emergency surgical procedure, long cross clamp period, and blood transfusion.[7] In this current study, we did not use risk factors in the Euro Score because this assessment is too weak to estimate mortality rate in high risk patients and combined coronary revascularization and valve surgery.[8] Euro Score accuracy differs among types of surgery. From six scoring systems, Euro Score had the highest predictive values although the morbidity predictive value differs from the mortality predictive values.[9]

In this study, most patients had pre-operative renal dysfunction with a mean creatinine clearance of 54.1 mL/minutes. Severe renal failure was found in 7.34%, which is higher than a previous report on 3154 patients which found that 2.1% of patients had severe renal failure requiring continuous renal replacement therapy.[10] Cardiac surgery and the use of heart-lung bypass machine may cause an inflammation response and induce acute renal failure.[11] Patients with mild pre-operative renal failure have a higher risk for developing post-operative renal failure and bleeding-associated re-surgery.[12]

In a study on 105 patients underwent cardiac surgery, mortality rate was 34.3% in those with pre-operative ejection fraction of 34.4%, using IABP support and mechanical ventilator of more than 24 hours.[1]Malnutrition increased the risk of morbidity and mortality after cardiac surgery. Observation on 15 patients with low BMI found that 5 out of 12 patients who underwent valve surgery and combined surgery died. This result was similar with another study who found that the risk of renal failure, pneumonia, re-surgery, bleeding, and brain ischemia was higher in patients with BMI less than 20 kg/m^2.[13]

An imbalance between renal oxygen supply and oxygen demand will induce acute renal failure. Oxygen supply in the kidney depends on the oxygen content in the renal blood flow. Renal blood flow will decrease if the mean arterial pressure is less than the renal optimal autoregulation value. Reduced renal blood flow will decrease glomerular filtration rate (GFR); which in turn, affect tubular oxygen reabsorption and then reduces renal oxygen consumption.[4] Renal blood flow reduction is a major cause of renal failure after cardiac surgery.[11] Our study showed that with a mean pre-operative hemoglobin levels of 11.4 g/dL and post operative hemoglobin levels of 8.97 g/dL, the risk of renal failure was high even when the arterial blood pressure was 76.2 mmHg. Patient with severe hypotension and anemia was more frequently experienced renal failure than hypotension without anemia.[14]

Mean cardiac bypass time in this study was 133.4 minutes. Several studies showed that long cardiac bypass time might cause red blood cell injury which release free hemoglobin along with transferrin, haptoglobin, and scavengers, causing renal tubular damage and death.[15] Normal venous oxygen saturation indicates that there is sufficient oxygen supply for the tissue. Low venous oxygen saturation, either due to insufficient oxygen supply or increased oxygen demand, may indicate that the body is under critical condition to keep the balance of oxygen.[5]

Patients with inotropic exposure showed less mortality rate than those without inotropic exposure. This result differed from other observation. In this study, the number of variables and sample size highly affects the real observed values.

Conclusion

In conclusion, there are several risk factors associated with renal failure requiring continuous renal replacement therapy after cardiac surgery. Pre-operative severe renal dysfunction, NYHA class IV heart failure, critical condition, coronary revascularization surgery, post-operative bleeding and anemia, and venous saturation less than 65% are independent variables that associated with mortality. Based on the principal component analysis, it can be estimated that re-surgery, bleeding and inotropic use may result in post-operative renal failure. These high-risk patients need to be optimally prepared before surgery in hoping that intra- and post-operative outcomes could be better and may reduce morbidity and mortality.

References

1. Castelli P,Condemi A,Munari M.Intra-aortric balloon counter pulsation:outcome in cardiac surgical patients. J CardiothoracVascAnesth. 2001;15:700-3.
2. Veli K, Faisal H, Cheema. Surgery for coronary artery disease. Coronary artery bypass grafting in patients with low ejection fraction. Circulation. 2005;112:344-50.
3. Hayashida N,Chihara S,Tayama E.Coronary.Coronary artery bypass grafting in patients with mild renal insufficiency.Jpn Circ J. 2001;65:28-32.
4. Haase M, Bellomo R, Story D, Letis A. Effect of mean arterial

pressure, haemoglobin and blood transfusion during cardiopulmonary bypass on post-operative acute kidney injury. Nephrol Dial Transplant.2011;0:1-8.
5. Edwards. Understanding continuous mixed venous oxygen saturation monitoring with the Swan-Ganz oximetry TD system.
6. Shahin J, DeVarennes B, Tse CW. The relationship between inotrope exposure, six-hour postoperative physiological variables, hospital mortality and renal dysfunction in patients undergoing cardiac surgery.Critical Care. 2011;15:R162.
7. Valdivieso JP, Monedero P, Vives M, Fernandez NG. Cardiac-surgery associated acute kidney injury requiring renal replacement therapy. A Spanish retrospective case-cohort study.BMC Nephrology. 2009;10:27.
8. Bhatti, Grayson AD, Grotte G, Fabri BM. The Logistic Euro SCORE in cardiac surgery: How well does it predict operative risk? Heart.2006;92(12):1817-20.
9. Hans JG, Phillip H, Sascha M. Risk stratification in heart surgery: comparison of six score systems. Eur J Cardio Thoracic Surg. 2000;17:400-6.
10. Bent P, Tan HK, Bellomo R. Early and intensive continuous hemofiltration for severe renal failure after cardiac surgery. Ann Thorac Surg. 2001;71:832-7.
11. Mehta R. Acute renal failure and cardiac surgery: marching in place or moving ahead? J Am Soc Nephrol. 2005;1
12. Caenegem OV, Jacquet LM. Outcome of cardiac surgery patients with complicated intensive care unit stay.CurrOpin Critical Care. 2002;8:404-10.
13. Engelman DT, Adams DH, Byrne JG.Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. J ThoracCardiovasc Surg. 1999;18:866-73.
14. Rosner M, Okusa MD. Acute kidney injury associated with cardiac surgery.Circulation. 2009;119:495-502.
15. Haase M, Bellomo R. Novel biomarkers, oxidative stress, and the role of labile iron toxicity in cardiopulmonary bypass-associated acute kidney injury. J Am CollCardiol. 2010;55:2024-33.