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Full Length Research Paper

Analysis of risk factors for acute kidney injury and in-hospital death following aortic arch surgery based on the RIFLE criteria

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The purpose of this study was to identify risk factors for acute kidney injury (AKI) and death of patients undergoing aortic arch surgery based on the RIFLE (risk, injury, failure, loss and end-stage kidney diseases) criteria. AKI was diagnosed according to the RIFLE criteria in patients undergoing aortic arch reconstruction with deep hypothermic circulatory arrest (DHCA). Clinical data of a total of 70 patients undergoing aortic arch reconstruction with DHCA from January 2009 to December 2009 were retrospectively reviewed. Known predictors (age, chronic kidney disease, surgery status, redo, diabetes, hypertension, blood transfusion, bypass, and deep hypothermic circulatory arrest time) were used in multivariate logistic regression analysis for acute kidney injury and in-hospital mortality. Thirty patients (42.9%) were diagnosed as Class I or F according to the RIFLE criteria, among which 10 patients (14.3%) required dialysis. The mortality rate was 11.4%. Risk factors for acute kidney injury included hypertension (odds ratio [OR] = 5.27), postoperative hypoxemia (OR = 13.36) and prolonged vasopressor dependence (OR = 12.49). Risk factors for mortality included AKI (RIFLE class F) (OR = 9.86), post liver dysfunction (OR = 6.42) and prolonged mechanical ventilation (OR = 11.76). AKI is a common complication after aortic arch surgery with DHCA. RIFLE classification provides with a useful diagnostic tool for AKI, and also the chance for further studies on prevention and treatment of AKI after DHCA.

Key words: Deep hypothermic circulatory arrest, aortic arch surgery, risk factors, acute kidney injury.

INTRODUCTION

Acute kidney injury (AKI) is one of the common complications during the peri-operative period of aortic arch reconstruction with deep hypothermic circulatory arrest (DHCA). It not only prolongs hospitalization duration, but also increases the medical expense and mortality. The RIFLE criteria referring to risk, injury, failure, loss and end-stage kidney disease which were established in 2004 by the Acute Dialysis Quality Initiative, incorporating both laboratory and clinical parameters to assess renal function have been validated in patients undergoing coronary artery bypass and valve surgery (Kuitunen et al., 2006). However, the incidence of renal dysfunction in that patient population was low with only 8.5% of patients meeting criteria for I or F classification (Kuitunen et al., 2006).

The RIFLE criteria system stratifies renal failure into 3 grades of increasing severity of AKI (risk, injury, failure) and 2 outcome classes (loss of kidney function, end-stage kidney disease). The 3 grades of severity for AKI can be based on changes in either plasma creatinine or urine output from baseline or both. RIFLE criteria have been validated in cardiac surgery (Machado et al., 2009; D'Onofrio et al., 2010) but the prevention and consequences of aortic arch surgery–associated AKI are still not well-established. Furthermore, risk factors for AKI defined with the RIFLE criteria still have not been

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Table 1. Surgical methods of aorta.

Surgical methods	n (%)
Replacement of aortic arch and ascending aorta.	8 (11.4)
Replacement of aortic arch and ascending aorta plus implantation of stent in descending aorta.	58 (82.9)
Implantation of stent in aortic arch and descending aorta.	2 (2.9)
Single replacement of aortic arch.	2 (2.9)

identified. The objective of our present study was to investigate whether the application of RIFLE criteria in diagnosing AKI was able to objectively predict the prognosis of patients with AKI. The associated risk factors of AKI were also analyzed.

PATIENTS AND METHODS

There were 71 patients undergoing aortic arch reconstruction with DHCA from January 2009 to December 2009, among which 1 patient was excluded because hemodialysis was performed before surgery for oliguria renal failure. There were 50 males (71.4%) and 20 females (28.6%), with a mean age of 50.94 ± 10.69 years (21 to 74 years). The co-morbidity included hypertension in 51 patients (72.9%), diabetes mellitus (DM) in 3 patients (4.2%), smoking history in 16 patients (22.9%), and renal dysfunction in 14 patients (20.0%). Dissecting aneurysm was classified into type I in 63 patients (88.7%), type II in 6 patients (8.5%), type III in 1 patient (1.4%) and pseudoaneurysm in 1 patient (1.4%). There were 56 patients (80.0%) with acute dissecting aneurysm and 26 patients (37.1%) had their surgeries performed emergently.

Surgical protocols are shown in Table 1. Total aortic arch replacement was performed in 22 patients, among which double valve replacement was performed in 1 patient, aortic valve replacement was performed in 11 patients and coronary artery bypass graft (CABG) was performed in 5 patients.

Diagnosis of postoperative AKI: AKI was classified into risk, injury, failure according to the RIFLE criteria. Postoperative hypoxemia was diagnosed as the ratio of arterial partial pressure of oxygen against inhalational oxygen concentration lower than 200. Delayed extubation was defined as assisted ventilation with respirator for longer than 72 h.

The patients were classified into 2 groups according to AKI: AKI group and non-AKI group. The potential risk factors were compared between the 2 groups, including age, gender, smoking history, hypertension, DM, cardiopulmonary bypass (CPB) duration, aortic clamping duration, DHCA duration, postoperative urine volume, creatinine value, GPT value, drainage volume, transfusion volume, duration of assisted ventilation, length of stay in ICU, hospitalization duration, stroke, mediastinal infection and in-hospital mortality.

Statistical analysis

All data were analyzed in SPSS 10.0. Numeration data was compared using chi-square test and measurement data was compared using t-test. Logistic regression analysis was used to analyze association between AKI, in-hospital mortality and the potential risk factors. $P< 0.05$ was considered statistically significant.

RESULTS

Postoperative AKI occurred in 47 out of the 70 patients (67.1%), with 17 patients of class R, 7 patients of class I and 23 patients of class F. Renal replacement therapy (RRT) was performed in 10 patients, among which 6 patients died and the mortality among patients underwent RRT was 60%. The total in-hospital mortality was 11.4% (8 patients). The cause of death included neurologic complications, renal failure, gastrointestinal tract hemorrhage and multiple organ dysfunction.

Univariate analysis of risk factors for AKI are shown in Table 2. No statistically significant difference was observed in gender, DM, emergent surgery, acute dissecting aneurysm, hepatic and renal function, DHCA duration, aortic clamping duration, CPB duration, urine volume and drainage volume on the first day after surgery, and re-thoracotomy between the 2 groups, while age, hypertension, postoperative hypoxemia, use of vasopressor for longer than 3 days, delayed extubation, prolonged length of stay in ICU, transfusion volume larger than 5 U were significantly associated with postoperative AKI.

Univariate analysis of death showed that risk factors for mortality included delayed extubation, postoperative stroke, AKI of Class I and F, mediastinal infection, postoperative hepatic dysfunction, hypoxemia and transfusion volume larger than 5 U.

Multivariate logistic regression analysis is shown in Tables 3 and 4. The independent risk factors of AKI included preoperative hypertension, postoperative hypoxemia, use of vasopressor after surgery for longer than 3 days and that of death included AKI of Class F, postoperative hepatic dysfunction and delayed extubation.

DISCUSSION

Acute renal failure (ARF) occurred in about 5 to 30% patients undergoing cardiac surgery (Lassnigg et al., 2008; Hobson et al., 2009), which is regarded as the strongest risk factor of death. However, clinical definition of ARF is confused without a unified diagnostic criterion. ARF definition is ranged from slight increase of creatinine to oliguria renal failure. Agreement of ARF definition is warranted for clinical investigation and treatment. Therefore, RIFLE classification was proposed by the ADQI group to evaluate the patient's condition according to the circulating creatinine, creatinine clearance rate and changes of urine volume. Five classifications were

Table 2. Univariate analysis of AKI.

	Total (N = 70)	Non-AKI group (N = 23)	AKI group (N = 47)	P value
Male	50 (71.4)	16 (69.6)	34 (72.3)	0.809
Female	20 (28.6)	7 (30.4)	13 (27.7)	0.809
Age	50.94 ±10.69	46.65 ±10.64	53.04 ± 10.18	0.018
Age>50	37 (52.9)	8 (34.8)	29 (61.7)	0.034
DM	3 (4.3)	0(0.0)	3 (6.4)	0.546
Hypertension	51 (72.9)	13 (56.5)	38 (80.9)	0.032
History of stroke	4 (5.7)	1 (4.3)	3 (6.4)	0.725
Preoperative abnormal Creatinine	14 (20.0)	5 (21.7)	9 (19.1)	0.799
Preoperative abnormal GPT	5 (7.1)	2(8.7)	3 (6.4)	0.728
Preoperative hypoxemia	4 (5.7)	1 (4.3)	3 (6.4)	0.725
Acute dissecting aneurysm	56 (80.0)	18 (78.3)	38 (80.9)	0.799
Emergent surgery	26 (37.1)	6 (26.1)	20 (42.6)	0.181
CPB duration	133 ± 49	120.91 ± 33.46	139.21 ± 54.41	0.144
Aortic clamping duration	55±26	57.65 ± 27.09	54.13 ± 25.05	0.592
DHCA duration	31±11	30.22 ± 12.14	31.20 ±10.49	0.730
Re-thoracotomy	3 (4.3)	1 (4.3)	2 (4.3)	0.986
TND	12 (17.1)	5 (21.7)	7 (14.9)	0.475
Stroke	18 (25.7)	3 (13.0)	15 (31.9)	0.077
Postoperative hypoxemia	26 (37.1)	2 (8.7)	24 (51.1)	0.000
Postoperative abnormal GPT	30 (42.9)	7 (30.4)	23 (48.9)	0.142
Mediastinal infection	7 (10.0)	1 (4.3)	6 (12.8)	0.239
Use of vasopressor for longer than 3 days	18 (25.7)	1 (4.3)	17 (36.2)	0.002
Delayed extubation	30 (42.9)	5 (21.7)	25 (53.2)	0.013
Drainage volume on the first day after surgery	513 ± 551	347 ± 287	591 ± 626	0.086
Length of stay in ICU	9.60 ±10.85	5.09 ± 4.85	11.81 ± 12.26	0.014
Length of stay in ICU longer than 5 days	35 (50.0)	6 (26.1)	29 (61.7)	0.005
Transfusion volume larger than 5U	15 (21.4)	2 (8.7)	13 (27.7)	0.054
Sepsis	8 (11.4)	1 (4.3)	7 (14.9)	0.161
Hospitalization duration	22.13 ±14.53	19.78 ± 9.46	23.28 ± 16.42	0.348
In-hospital mortality	8 (11.4)	1 (4.3)	7 (14.9)	0.161

Table 3. Independent risk factors for AKI in multivariate logistic regression analysis.

	Odd ratio (OR)	95% Confidence interval	P value
Preoperative hypertension	5.27	1.23 - 22.67	0.026
Postoperative hypoxemia	13.36	2.29 - 77.93	0.004
Use of vasopressor after surgery for longer than 3 days	12.49	1.28 - 121.86	0.030

Table 4. Risk factors for death in multivariate logistic regression analysis.

	Odd ratio (OR)	95% Confidence interval	P value
AKI of Class F	9.86	2.06 - 47.21	0.004
Postoperative hepatic dysfunction	6.42	1.17 - 35.10	0.032
Delayed extubation	11.76	1.82 - 76.11	0.010

defined according to RIFLE criteria, included 3 classes of severity (risk, injury and failure) and 2 classes of clinical outcome (loss of renal function and end-stage nephropathy). Most of current studies were focus on RIFLE classification in valve replacement surgery and coronary artery bypass graft (CABG) and that in aortic

arch surgery was seldom reported.

Incidence of AKI was high after aortic arch surgery. AKI not only prolonged hospitalization duration, but increased medical expense and mortality because of fatal complications, such as sepsis, gastrointestinal hemorrhage and neurologic complications. Arnaoutakis et al. (2007) found that mortality was increased with the elevation of RIFLE classification (RIFLE class 0 = 3%, R = 9%, I = 12% and F = 38%). The proportion of patients requiring hemodialysis was as high as 30 to 60%. It was demonstrated by the present study that only AKI of Class F was associated with death and mortality in dialysis patients was as high as 60%. Thus monitor and evaluation of renal function at the early stage was a great challenge for critical care physicians to reduce the mortality.

It was reported in previous studies that risk factors of AKI included age, chronic nephropathy, emergent surgery, re-thoracotomy, DM, hypertension, transfusion volume, CPB and DHCA durations (Arnaoutakis et al., 2007; Karkouti et al., 2009). The present study showed that preoperative history of hypertension, postoperative hypoxemia and use of vasopressor after surgery for longer than 3 days were risk factors of AKI after aortic arch surgery.

The pathologic mechanisms of AKI include renal tubular necrosis induced by ischemia, injury and activetion of vascular endothelium. Normally, renal perfusion is self-regulated. Glomerular filtration rate does not reduce until the mean arterial pressure was lower than 80 mmHg. However, self-adjustment capacity may be impaired in patients with older age, vascular sclerosis, hypertension, chronic renal dysfunction, hemodynamic instability and preoperative use of non-steroidal anti-inflammatory drugs, ACE inhibitors, angiotensin receptors blockers and contrast media (Cosmi et al., 2000). In these conditions, renal function might be deteriorated even if blood pressure was within the normal range. What's more, inflammatory system is activated by CPB and DHCA, followed by activation of complement and release of inflammatory factors, activation of sympathoadrenal system and renin-angiotensin-aldosterone system, ischemic reperfusion injury, production of free hemoglobin and ferrum induced by haemolysis, and finally, AKI is induced.

Among the 3 risk factors for AKI in the present study, preoperative hypertension predicts the impaired capacity of renal self-adjustment and poor tolerance against ischemia and hypoxia. Vasopressors were used for longer than 3 days because myocardial ischemia, system inflammation response and reduced systemic vascular resistance were induced with the prolongation of CPB duration. Meanwhile, dependence on vasopressors demonstrated the instable hemodynamic condition. Therefore, the risk factors of AKI are in accordance with the pathologic mechanisms of AKI.

Measures should be applied early after surgery to prevent AKI in patients with preoperative hypertension, postoperative hypoxemia and vasopressor dependence. The measures include close monitoring of renal function and urine volume, protection and improvement of cardiac function, early recovery of hemodynamic condition, prevention of cardiac pulmonary edema, prolonging use of respirator, prevention of pulmonary infection and hypoxemia (Augoustides et al., 2006). Anti-inflammatory medications may also be helpful, such as ulinastatin and methylprednisolone. RRT should be performed when necessary to maintain water and electrolytes balance, elimination of circulating nitrogen metabolite, improve hemodynamic status and recovery of renal, pulmonary and neurologic function.

In summary, risk factors of AKI after aortic arch surgery with DHCA include preoperative hypertension, postoperative hypoxemia and use of vasopressor after surgery longer than 3 days. The RIFLE classification provides an opportunity for early diagnosis and treatment of AKI, as well as improving prognosis. It is very important for clinical physicians to investigate how to predict the outcome, choose suitable treatment and improving prognosis. Further studies should be performed for alleviation or treatment of risk factors of AKI.

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