Risk Factors for Acute Kidney Injury Requiring Continuous Renal Replacement Therapy after Off-Pump Coronary Surgery

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Abstract

Background: Recently, off-pump coronary artery bypass (OPCABG) grafting without cardiopulmonary bypass has become a less stressful surgical procedure for coronary artery bypass grafting (CABG). Many reports have discussed the risk factors involved associated with on-pump coronary artery bypass grafting and acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT). However, only a few papers have evaluated the risk factors for AKI requiring CRRT after OPCABG.

Aim: The purpose of this study was to assess the risk factors for AKI requiring CRRT after OPCABG.

Methods: An observational study of 237 consecutive non dialysis patients who underwent isolated CABG using OPCABG was conducted from September 2010 to June 2012. AKI was defined as proposed by the Acute Kidney Injury Network. Variables with P<0.05 in bivariate analysis collected from pre-, intra- and postoperative data were tested in the multivariate and proportional hazards regression analyses for risk factors of AKI requiring CRRT after OPCABG.

Results: Among 237 subjects, 33 patients needed CRRT due to AKI. The risk factors that were independently associated with AKI requiring CRRT were: pre-estimated glomerular filtration rate (GFR) (less than 60 ml/min/1.73m²), pre-serum albumin level (less than 3.5 g/dl), pre-hemoglobin level (less than 12g/dL), intra-urine volume (less than 600 mL), use of intra-aortic balloon pump (IABP), and post-PaO₂/FiO₂ (P/F) (less than 300).

Conclusion: In conclusion, it is possible that the risk of developing AKI requiring CRRT after OPCABG depended on the levels of GFR, serum albumin and hemoglobin before surgery, on the levels of urine volume and use of IABP during surgery and the levels of P/F after surgery.

Keywords: eGFR; Albumin; Hemoglobin; IABP

Introduction

Acute kidney injury (AKI) has been reported to occur in 30% to 40% of patients undergoing cardiac surgery [1]. Patients with AKI requiring continuous renal replacement therapy (CRRT) have mortality rates in excess of 40% to 50% [2]. To avoid postoperative complications, off-pump coronary-artery bypass grafting (OPCABG) has recently been utilized [3]. Although randomized trials of OPCABG have not demonstrated benefits, reductions in the incidence of AKI were demonstrated [4,5,6]. Previously Thakar et al. [7] proposed a clinical score to predict AKI after cardiac surgery. However, their study was not clear on risk factors in patients undergoing OPCABG. Besides, it has been reported that the risk of AKI requiring CRRT varies substantially among different types of cardiac surgical procedures [8,9]. There are large discrepancies among reports on long-term survival in cardiac surgical patients treated with CRRT, varying from 10% at 1 year to 52% at 5 years [10,11,12]. The identification of risk factors for AKI in patients after OPCABG may result in better care, more appropriate resource utilization, and, finally, better outcome. The purpose of this study was to determine the risk factors that predict AKI requiring CRRT after OPCABG.

Methods

All adult patients who developed AKI-CRRT in the postoperative cardiac surgical intensive care unit at a single academic center from September 2010 through June 2012 were included in this retrospective case-control study. Patients excluded from the study were: 1) those with severe chronic renal failure, which was defined by less than 15 ml/min/1.73m² (CKD stage 5) or chronic dialysis therapy; 2) history of chronic obstructive pulmonary disease requiring medical therapy; 3) previous open-heart surgery; and 4) those who died during the first 24 hours after surgery were excluded because these patients died either from acute heart failure or bleeding in direct consequence of cardiac surgery.

Definitions

The AKI was defined according to the Second International Consensus Conference of the Acute Dialysis Quality Initiative Group [13] with reference to RIFLE (risk, injury, failure, loss, and end-stage kidney disease) using the criteria for kidney injury [14]. The primary outcome was AKI that required dialysis during the postoperative period. CRRT was carried out as continuous venovenous hemofiltration (CVVHDF) and was started when at least one of the following institutional protocol requirements was fulfilled: 1) urine output below 0.5 ml/kg/h in 6 hours despite treatment with fluid transfusion, inotropes, and/or vasoconstrictor infusions aimed at optimization of the hemodynamic parameters and the administration of furosemide 100 mg/h over 3 hours or 2) more than a 4-fold increase in plasma creatinine concentration was observed. Hemofiltration treatment

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ceased when patients recovered urine output exceeding 1 mL/kg/h, provided that no indications for RRT were observed subsequently. Patients were accessed through double-lumen catheters (Vas-cath, Medicon Co., Chicago, IL), which were inserted into the right or left femoral vein and connected to a continuous hemodialyzer (KIM6000, Kurary Co. Ltd., Tokyo, Japan). An anticoagulant, nafamostat mesilate (Futhan, Torii Pharmaceutical Co. Ltd., Tokyo, Japan), was used at 30 IU/hr. CRRT was started under conditions of water elimination rate of 60 mL/hr, dialysate (HF Solita, Shimizu Pharmaceutical Co., Ltd., Shimizu, Japan) flow rate (Qd) of 16 mL/min, blood flow rate (Qb) of 100 mL/min and predilution replacement solution flow rate (Qpre) of 30 mL/min. The dialyzers used in this study were Panflow APF-S (Asahi Medical Co., Ltd., Tokyo, Japan) and Hemofeel SH (Toray Medical Co., Ltd., Tokyo, Japan). Both preoperative and intraoperative variables were examined for possible predictors of AKI to develop the scoring model. Preoperative: age, gender, body mass index (BMI), ejection fraction, diabetes mellitus evaluated by hemoglobin A1C, preoperative estimated glomerular filtration rate (eGFR) (eGFR was calculated using a modified three-variable equation for eGFR in Japanese patients: eGFR=194xage-0.287 x SCr -1.094(x0.739, if female), where SCr=serum creatinine [15] and preoperative levels of serum albumin, hemoglobin, and C-reactive protein (CRP) as indication of inflammation. Intraoperative: emergency surgery, use of intra-aortic balloon pump during surgery, number of grafted coronary vessels, cardiopulmonary bypass (CPB) time, urine volume, and doses of furosemide. The following intraoperative data were also recorded: mean arterial pressure (mm Hg), doses of catecholamines (μg/kg/min), cardiac index (L/min/m²), central venous pressure (cmH₂O), and PaO₂/FiO₂. The rationale for using these variables in the scoring model was based on the findings reported by Thaker et al. [7].

Statistical Analyses

Data were analyzed by using SAS 1999 program (release 8.00 by SAS Institute Inc, Cary, NC). Continuous measures are expressed as mean ± standard deviation or as median (50th percentile) and compared with a “t-test” for unpaired data, as appropriate. Comparison of continuous variables between the two groups was performed with the Mann-Whitney’s U test, and categorical data were analyzed by using Fisher’s exact test. Variables with univariate significance P<0.001 were identified and then the following variables were used as dichotomous variables: Preoperative: age, 65 years; eGFR, 60 mL/min/1.73 m²; albumin, 3.5g/dL; hemoglobin, 12 g/dL; and CRP, 0.5 mg/dL. These values were arbitrarily determined with the following reasons; in Japan, elderly people are defined as 65 years and over. Also, less than 60 mL/min/1.73m² is defined as CKD. The anemia was defined less than 12.0g/dL. The lower limit of serum albumin was 3.5g/dL.

Intraoperative: presence of IABP; catecholamine index, 5 μg/kg/min; urine volume, 600 mL; and use of furosemide. Postoperative: mean arterial pressure, 70 mm Hg; and P/F ratio, 300 using sequential organ failure assessment (SOFA) score. These variables for AKI requiring CRRT identified by univariate logistic regression analysis were further tested by multivariate regression. Score points were assigned to each risk factor using regression coefficients and rounded to the nearest integer. Receiver operating characteristic plots of the score models predicting AKI requiring CRRT were produced.

Results

(Table 1) shows the characteristics of all patients. The variables including age, preoperative CRP, requiring emergency operation, use of IABP, use of furosemide during surgery, doses of catecholamine (CAI) during surgery, and postoperative PaO₂/FiO₂ (P/F) were significantly higher in patients requiring CRRT. In contrast, variables including preoperative eGFR, preoperative serum albumin and hemoglobin, urine volume during surgery, and postoperative mean arterial pressure were significantly lower in patients requiring CRRT. In (Table 2), univariate analysis was performed to identify risk factors for AKI requiring CRRT and analysis of simple regression of these variables are shown. Significant associations with AKI were shown for eGFR, ALB, HGB, IABP, urine volume, and P/F ratio. The analysis was

| Pre                                | ALL(n=237) | Non RRT(n=204) | RRT (n=33) | p-value |
|------------------------------------|------------|----------------|------------|---------|
| Age(yr)                            | 70 [64~75] | 69 [63~75]     | 73 [67~80] | .021    |
| Sex(M:F)                           | 173 ±64    | 152 ±52        | 21 ±12     | .207    |
| BMI(kg/m²)                         | 23.2 [20.6~25.3] | 23.2 [20.5~25.3] | 23.1 [21.3~25.4] | .487    |
| HbA1c(%)                           | 5.8 [5.3~6.7] | 5.7 [5.3~6.8]  | 6 [5.4~6.7] | .581    |
| Ejection fraction (%)              | 53 [42~64] | 54 [43~66]     | 48 [33~59] | .061    |
| eGFR(mL/min/1.73m²)                | 58.3 [47.2~74.2] | 62.6 [50.8~76.2] | 26.9 [19.4~47.5] | <.001   |
| ALB(g/dL)                          | 3.8 [3.4~4.15] | 3.9 [3.5~4.2]  | 3.4 [3.1~3.7] | <.001   |
| HGB(g/dL)                          | 12.2 [10.9~13.6] | 12.5 [11.2~13.9] | 10.5 [9.5~11.9] | <.001   |
| CRP(mg/dL)                         | 0.24 [0.07~0.97] | 0.22 [0.07~0.83] | 0.60 [0.10~2.23] | .043    |
| Emergency                          | 80(25%)    | 43(21%)        | 17(51.5%)  | <.001   |
| IABP(%)                            | 66(28%)    | 48(25.5%)      | 18(54.5%)  | <.001   |
| Number of vessels(number)          | 3(3~4)     | 3(3~4)         | 3(3~4)     | .477    |
| Duration of anesthesia(Hr)         | 6.93 [5.68~7.63] | 7.0 [5.95~7.55] | 6.35 [5.55~7.81] | .646    |
| Urine volume(mL)                   | 700 [450~1050] | 730 [485~1075] | 450 [300~590] | <.001   |
| furosemide                         | 42(18%)    | 28(14%)        | 14(42.5%)  | .01     |

| Post                               | ALL(n=237) | Non RRT(n=204) | RRT (n=33) | p-value |
|------------------------------------|------------|----------------|------------|---------|
| Mean arterial pressure (mmHg)      | 68 [63~75] | 68.5 [63~75]  | 64 [58~69] | .002    |
| CAI(μg/kg/min)                     | 4.1 [2.0~7.42] | 3.94 [1.98~7.36] | 5.8 [2.76~9.45] | .043    |
| Cardiac index(L/min/m²)            | 2.4 [2.1~2.8] | 2.4 [2.2~2.8]  | 2.3 [2.05~2.75] | .245    |
| Central venous pressure            | 7.0 [5~10]   | 7.0 [5~9.8]   | 8.0 [5.5~10]  | .540    |
| (cmH₂O) P/F ratio                  | 309 [256~371] | 316 [260~374]  | 262 [199~313] | <.001   |

Values are expressed as mean ± standard deviation. BMI: body mass index; ALB: serum albumin; eGFR: estimated glomerular filtration; HGB, hemoglobin; CRP: C-reactive protein; IABP: intra-aortic balloon pumping; CAI: catecholamine index; P/F, PaO₂/FiO₂.

Table 1: Characteristics of the patients.
Discussion

The present study demonstrated that risk factors for AKI requiring CRRT after OPCABG were preoperative eGFR, ALB, HGB, urine volume and use of IABP during surgery and postoperative P/F ratio. Recently, Kiers et al. [16] compared the predictive value of eight models reported up to 2011. They found a significant relationship with CRRT after OPCABG were preoperative eGFR, ALB, HGB, urine volume and use of IABP during surgery and postoperative P/F ratio. Compared to the previous data, our analysis revealed that preoperative levels of ALB and HGB were independent risk factors for AKI requiring CRRT after OPCABG. These factors were not extracted from the previous studies. In our models, the cut off levels of ALB and HGB were 3.5 g/dL and 12 g/dL, respectively. It is generally uncommon for patients with CKD stage 3a to have levels of ALB less than 3.5 g/dL and for HGB of less than 12 g/dL. Our analysis clearly demonstrated that slightly lower levels of albumin and hemoglobin should be recognized as predictors for development of AKI requiring CRRT in conjunction with reduced eGFR. In the present study, we excluded patients with eGFR of less than 15 ml/min/1.73 m² (CKD stage 5 without dialysis). The factors extracted from our study eg, use of IABP and reduction of urine volume are closely associated with combination of low cardiac output and reduction of renal function. This combination

| Risk factors        | Regression coefficient | Odds ratio (95% CI) | p-value |
|---------------------|------------------------|--------------------|---------|
| Age (yr)            | 0.531                  | 1.060(1.012 ~ 1.112) | .013    |
| eGFR (mL/min/1.73m²) | -2.262                 | 0.903(0.875 ~ 0.932) | < .001  |
| ALB (g/dL)          | -0.914                 | 0.183(0.086 ~ 0.387) | < .001  |
| HGB (g/dL)          | -1.048                 | 0.838(0.461 ~ 0.739) | < .001  |
| CRP (mg/dL)         | 0.422                  | 1.192(1.058 ~ 1.343) | .003    |
| emergency           | 0.600                  | 3.978(1.858 ~ 8.515) | < .001  |
| IABP                | 0.610                  | 3.900(1.828 ~ 8.320) | < .001  |
| Urine volume (mL)   | -1.281                 | 0.997(0.996 ~ 0.999) | < .001  |
| furosemide          | 0.585                  | 4.631(2.086 ~ 10.27) | < .001  |
| Mean arterial pressure (mmHg) | -0.577 | 0.936(0.890 ~ 0.985) | .11     |
| CAI (μg/kg/min)     | 0.449                  | 1.093(1.028 ~ 1.163) | .005    |
| P/F ratio           | -0.724                 | 0.991(0.986 ~ 0.999) | < .001  |

Table 2: Univariate analysis for AKI patient requiring CRRT.

| Risk factors          | Regression coefficient | Odds ratio (95% CI) | p-value |
|-----------------------|------------------------|--------------------|---------|
| Pre eGFR< 60mL/min/1.73m² | 2.545                  | 2.711              | 3.184  |
| Pre HGB < 12g/dL       | 1.313                  | 0.574              | 1.207  |
| Pre ALB < 3.5 g/dL     | 1.146                  | 0.142              | 1.114  |
| Pre ALB < 3.5 g/dL     | 1.146                  | 0.142              | 1.114  |
| Pre IABP < 1000        | 1.166                  | 0.522              | 1.894  |
| Intra urine volume < 600 mL | 1.490              | 0.533              | 1.561  |
| Intra urine volume < 600 mL | 1.490              | 0.533              | 1.561  |
| Intra use of IABP     | 1.146                  | 0.517              | 1.142  |
| Post P/F ratio < 300   | 1.146                  | 0.517              | 1.142  |

Table 3: Multiple logistic regression analysis.

| Points                  | 1                   |
|-------------------------|---------------------|
| Pre ALB < 3.5 g/dL      | 1                   |
| Pre eGFR< 60mL/min/1.73m² | 2                   |
| Pre HGB < 12g/dL        | 1                   |
| Intra urine volume <600 mL | 1                   |
| Intra use of IABP      | 1                   |
| Post P/F Ratio < 300    | 1                   |

Table 4: Score for risk factors.

Figure 1: Frequency of AKI requiring CRRT corresponding to risk score.

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coronary artery bypass depended on the levels of GFR, serum albumin and hemoglobin before surgery, on the levels of urine volume and use of IABP during surgery and the levels of P/F after surgery.

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The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Conflict of Interest

The authors declare no conflict of interest in this study.

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