Use of cerebral oxygen saturation and hemoglobin concentration to predict acute kidney injury after cardiac surgery

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Abstract
Objective: Acute kidney injury (AKI) is a common complication after cardiac surgery and is associated with significant morbidity and mortality. Near infrared spectroscopy (NIRS) is a non-invasive technique for real-time measurement of cerebral tissue oxygenation. The purpose of the present study was to evaluate the correlation of AKI with hemoglobin and regional cerebral oxygen saturation (rScO₂) measured intraoperatively and postoperatively in patients undergoing cardiac surgery.

Methods: We retrospectively analyzed the prospectively collected data of 45 adult patients with normal renal function who underwent isolated coronary artery bypass grafting (CABG) from January 2014 to May 2014. Kidney injury was assessed according to the Acute Kidney Injury Network criteria. rScO₂ and hemoglobin were measured every hour intraoperatively and for the first 24 hours postoperatively.

Results: The hemoglobin concentration and rScO₂ were significantly lower in patients with than without AKI, and no linear trends were observed. No exact cut-off values were obtained.

Conclusion: This retrospective study shows that a lower rScO₂ and hemoglobin concentration are correlated with AKI after CABG in patients with no peripheral vascular disease or recent myocardial infarction. We suggest that cerebral oximetry alone may predict postoperative AKI well.

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Introduction

Acute kidney injury (AKI) is a common complication after cardiac surgery and is associated with significant morbidity and mortality.\(^1\) It also results in high costs due to a long hospital stay.\(^2\) The incidence of AKI ranges from 1% to 40%.\(^3\)\(^-\)\(^5\) Severe arteriosclerosis of the aorta, high age, diabetes mellitus, preexisting renal dysfunction, impaired left ventricular function, and hypertension are the known major risk factors for the development of AKI after cardiac surgery.\(^6\)\(^-\)\(^8\) Intraoperative nonpulsatile flow, systemic inflammatory response syndrome, and renal hypoperfusion are important risk factors for postoperative AKI.\(^9\)\(^,\)\(^10\) Near infrared spectroscopy (NIRS) noninvasively demonstrates real-time degradation of tissue oxygenation, allowing necessary interventions to be performed in a timely manner.

NIRS is a noninvasive technique for real-time measurement of regional cerebral oxygen saturation (\(r\)ScO\(_2\)).\(^11\) NIRS measures the near-infrared wavelengths absorbed by oxygenated and deoxygenated hemoglobin.\(^12\) Low ScO\(_2\) values reportedly suggest systemically impaired tissue perfusion.\(^13\)\(^,\)\(^14\) A significant decrease in \(r\)ScO\(_2\) predicts poor outcomes in both cardiac and noncardiac surgical patients.\(^15\)

The purpose of the present study was to evaluate the correlation of AKI with \(r\)ScO\(_2\) and hemoglobin measured intraoperatively and continued for at least 24 hours postoperatively in patients undergoing cardiac surgery.

Methods

Patients

Our institutional review board approved the present study, and all patients had previously granted permission for use of their medical records for research purposes. We retrospectively analyzed the prospectively collected data of adult patients with normal renal function (baseline serum creatinine concentration of \(<1.4 \text{ mg/dL}\)) who underwent isolated coronary artery bypass grafting (CABG) from January 2014 to May 2014. Data of patients with preexisting sepsis, chronic renal failure being treated by hemodialysis or peritoneal dialysis, multiple organ failure, peripheral vascular disease, or recent myocardial infarction and patients undergoing either emergent surgery or operations other than or in conjunction with CABG were excluded from the study.

Kidney injury was assessed according to the Acute Kidney Injury Network (AKIN) criteria, which involve calculation of the serum creatinine concentration and urine output.\(^15\) Kidney injury was classified as stage 1, stage 2, or stage 3 (Table 1).

NIRS and CABG procedure

We used an INVOS monitor (Somanetics Covidien, Medtronic, Minneapolis, MN, USA) to measure \(r\)ScO\(_2\) intraoperatively and for 24 hours postoperatively. The INVOS sensors were placed on both the left and right forehead for \(r\)ScO\(_2\) measurement after intubation. All operations were
performed with a standardized approach using a Terumo roller pump (Terumo Advanced Perfusion System 1; Terumo Cardiovascular Group, Ann Arbor, MI, USA) and membrane oxygenators (Dideco Compactflo Evo; Sorin Group, Arvada, CO, USA). Mild to moderate hypothermia (28°C–32°C) and pulsatile flow of 2.2 to 2.4 L/m² were used. Myocardial protection was achieved with tepid antegrade blood cardioplegia, and a “hot shot” (250–500 mL) was delivered immediately prior to removal of the aortic cross clamp. The perfusion pressure was maintained at >70 mmHg at all times. Induction and maintenance of general anesthesia with endotracheal intubation were standardized for all patients (fentanyl, midazolam, and desflurane in oxygen with air). The same surgical team performed all operations.

After intubation, the rScO₂ was continuously recorded every 2 minutes during cardiopulmonary bypass until the end of the operation. The rScO₂ was then continuously recorded in the intensive care unit (ICU) for at least 24 hours postoperatively. A blood transfusion was considered when the intraoperative or postoperative hemoglobin concentration was <9 g/dL.

### Postoperative management

Postoperatively, the patients were followed in the ICU according to the protocols of our institution. Electrocardiography, systemic mean arterial pressure, central venous pressure, pulmonary artery and wedge pressures, cardiac output and index, arterial blood gases, chest tube output, and hourly urine output were monitored. Serum electrolytes were measured in conjunction with arterial blood gas measurement. Fluid and electrolyte imbalances were corrected immediately with appropriate management. A blood transfusion was considered when the hemoglobin concentration was <9 g/dL.

The blood urea nitrogen, serum urea and creatinine, and serum electrolyte concentrations were measured daily in all patients until discharge from the hospital. Preoperative and postoperative creatinine clearance and peak creatinine clearance were calculated according to the formulas reported in the literature.¹¹,¹⁶ Our staff nephrologists determined the indication criteria for renal replacement therapy (RRT) for the patients undergoing CABG. These criteria included hyperkalemia (potassium

| Stage | Serum creatinine criteria | Urine output criteria |
|-------|---------------------------|-----------------------|
| 1     | Increase to ≥26.5 μmol/L (≥0.3 mg/dL) OR increase of ≥150% to 200% (1.5× to 2×) | <0.5 mL/kg/h for >6 h |
| 2     | Increase of ≥200% to 300% (>2× to 3×) | <0.5 mL/kg/h for >12 h |
| 3ᵃ    | Increase to ≥353.6 μmol/L (≥4.0 mg/dL) OR baseline concentration of ≥353.6 μmol/L (≥4.0 mg/dL) | <0.3 mL/kg/h for >24 h |
|       | Increase to ≥44.2 μmol/L (≥0.5 mg/dL) | OR anuria for >12 h |

ᵃStage 3 also includes patients requiring renal replacement therapy independent of the stage

**Hemoglobin**

The hemoglobin and INVOS values were routinely and simultaneously measured every hour during the operation in accordance with the anesthesia protocol. These measurements were continued for 12 hours postoperatively.
of >6 mmol/L), anuria or oliguria (urine output of <0.5 mL/kg/h for 12 hours), and metabolic acidosis.

**Statistical analysis**

All statistical analyses were performed using SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA). A power analysis was also performed. Continuous variables are expressed as mean ± standard deviation and were compared by the unpaired Student's t test or Pearson's chi-square test. The effect of cerebral oxygen levels on AKI after CABG was determined using logistic regression analysis, and the results are expressed as the odds ratio with 95% confidence interval. A p value of <0.05 was considered statistically significant.

**Results**

In total, 45 adult patients were evaluated in this study. The patient demographics and operative data are shown in Table 2. Postoperative AKI occurred in 12 (26%) patients. The INVOS data recorded at all patients are summarized in Table 3. Compared with the baseline values, both the left and right cerebral oximetry values were significantly lower at 2 and 6 hours after cardiopulmonary bypass (left, p = 0.001 and p = 0.008, respectively; right, p = 0.009 and p = 0.001, respectively). No correlation was found between a reduction in rScO2 and AKI severity. Logistic regression analysis showed that lower cerebral oximetry levels were associated with a higher incidence of postoperative AKI (odds ratio, 0.667; 95% confidence interval, 0.485–0.917; p = 0.013). The preoperative mean serum creatinine concentration was 0.89 ± 0.19 mg/dL. Three patients had AKIN stage 1 AKI, seven patients had AKIN stage 2, and two patients had AKIN stage 3. RRT was performed in two (4%) patients. The creatinine

| Table 2. Perioperative INVOS values | Baseline | During CPB | 2 h after CPB* | 6 h after CPB** | 24 h after CPB |
|-------------------------------------|----------|-----------|---------------|----------------|---------------|
| Side                                | R        | L         | R             | L              | R             |
| rScO2                               | 63.84±7.50 | 63.76±7.50 | 63.58±7.68 | 63.56±8.28 | 60.09±7.64 |
|                                      | 63.58±7.68 | 63.56±8.28 | 63.58±7.68 | 63.56±8.28 | 60.09±7.64 |
|                                      | 60.09±7.64 | 60.09±7.64 | 60.09±7.64 | 60.09±7.64 | 60.09±7.64 |

Data are presented as mean ± standard deviation.

*Significant difference between baseline values and 2-hour post-CPB cerebral oximetry levels (p = 0.001 for left side and p = 0.009 for right side).

**Significant difference between baseline values and 6-hour post-CPB cerebral oximetry levels (p = 0.001 for left side and p = 0.001 for right side).

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concentration before commencement of RRT was 3.86 ± 0.71 mg/dL. RRT was started 50 to 55 hours after surgery and used for 5 to 6 days in these two patients. The mean creatinine concentration was 1.24 ± 0.89 mg/dL prior to hospital discharge. No patients became hemodialysis-dependent, and no patients required intra-aortic balloon pump support. Prolonged ventilatory support was necessary in 4.4% of patients who also required RRT.

The mean ICU stay was 35.63 ± 10.74 hours in patients without AKI; however, it was 115.83 ± 25.70 hours in patients who developed AKI (p < 0.001). The in-hospital stay was 6.57 ± 2.13 days in patients without AKI and 11.50 ± 3.75 days in patients with AKI (p = 0.011). One (2%) of the patients who required RRT died of low cardiac output. The ICU stay and in-hospital stay were not prolonged in patients with stage 1 AKI. The length of stay was not prolonged in the two patients who underwent RRT because RRT was started as soon as possible.

The mean preoperative urine output level was 0.7 ± 0.2 mL/h, and the mean serum osmolality was 293 ± 2 mOsm/kg. All patients were exposed to a radiopaque substance during coronary angiography, and no patients were undergoing angiotensin-converting enzyme inhibitor treatment.

The mean euroSCORE was 3.2% ± 1.5%.

The rSco2 and average mean arterial pressure among patients with and without postoperative AKI are shown in Table 4.

### Discussion

Brain and kidney injury are devastating complications after cardiac surgery. Kidney injury is associated with in-hospital mortality. The cerebral blood flow is autoregulated to satisfy the metabolic needs of the brain tissue. The renal blood flow is autoregulated to control bodily...
toxins and fluid balance and to preserve the glomerular structure. Despite these brain and renal autoregulation mechanisms, brain and renal tissue may be disrupted during CABG. Monitoring of brain tissue oxygenation is advised during CABG. Among the methods available for such monitoring, we used NIRS in the present study. NIRS is a noninvasive technique that allows for measurement of the oxygenation state of hemoglobin and mitochondrial cytochromes. The oxygenation status of cytochromes along the electron transport chain appears to provide the best estimate of cellular oxygenation. The technology for such measurement has been incorporated into devices capable of measuring the blood oxygen saturation in the brain.

Brain tissue oxygenation may reflect renal tissue oxygenation. In the present study, the incidence of AKI was higher than expected in patients with low rScO2. We determined that the rate of AKI development was higher in patients with low rScO2 and hemoglobin levels. These results indicate that in patients with low ScO2, the oxygen perfusion of other tissues may also be low. The hospital stay was also long in these patients. We determined that the mean rScO2 was significantly lower at 2 and 6 hours after cardiopulmonary bypass. This situation may be associated with impaired cardiac function and low hemoglobin concentrations in the early phase of CABG because in patients with lower hemoglobin concentrations, the rScO2 also decreased and AKI developed.

Erythrocyte replacement may be necessary to increase the oxygen carrying capacity when the rScO2 is low in the operating room and later in the postoperative period. In our opinion, volume replacement and administration of inotropic agents may also be necessary in these patients.

The rScO2 was low in patients with low hemoglobin concentrations. A low hemoglobin concentration decreases the tissue oxygen transport capacity and rScO2. Decreased oxygen transport capacity to the tissue also increases the incidence of AKI.

Again, the development of AKI in these patients was much higher. Rifai at al. suggested that rScO2 is an important biomarker in patients with heart failure and

Table 4. rScO2 and average MAP in patients with and without postoperative AKI

|                          | AKI (n = 12)          | No AKI (n = 33)         |
|--------------------------|-----------------------|-------------------------|
| Baseline rScO2 (%) (right)| 63.84 ± 4.60 (64–67) | 64.74 ± 5.64 (65–68)   |
| Baseline rScO2 (%) (left) | 64.74 ± 4.70 (64–67) | 64.74 ± 5.64 (65–68)   |
| rScO2 (%) (right) 2 h after CPB | 60.56 ± 5.6 (56–62)    | 69.84 ± 7.64 (65–70)    |
| rScO2 (%) (left) 6 h after CPB | 59.67 ± 5.5 (60–63)    | 62.84 ± 7.53 (65–66)    |
| MAP (mmHg) during CPB     | 60.5 ± 7.3 (64–74)     | 72.0 ± 7.5 (70–75)      |
| pH 2 h after CPB          | 7.37 ± 0.93            | 7.33 ± 0.02             |
| PaCO2 (mmHg) 2 h after CPB| 43 ± 3                 | 42 ± 5                  |
| PaO2 (mmHg) 2 h after CPB  | 278 ± 47               | 279 ± 49                |
| pH 6 h after CPB          | 7.46 ± 0.78            | 7.36 ± 0.14             |
| PaCO2 (mmHg) 6 h after CPB| 44 ± 1                 | 41 ± 12                 |
| PaO2 (mmHg) 6 h after CPB  | 260 ± 32               | 268 ± 38                |
| Hemoglobin (g/dL)         | 8.1 ± 1.1              | 9.7 ± 1.9               |
| Peak temperature during rewarming (°C) | 34.2 ± 2.1             | 34.6 ± 2.1              |

Data are presented as mean ± standard deviation (95% confidence interval).
AKI, acute kidney injury; rScO2, regional cerebral oxygen saturation; MAP, mean arterial pressure; CPB, cardiopulmonary bypass; PaCO2, partial pressure of arterial carbon dioxide; PaO2, partial pressure of arterial oxygen.
suggested that it may be a useful marker of target organ perfusion. Thus, rScO₂ as a measurement of cumulative oxygen desaturation acts as a predictor of the likelihood of intraoperative and postoperative complications.

In this study, the rate of postoperative AKI development was high in patients with a low rSO₂. AKI developed postoperatively in 12 patients, and their rScO₂ levels were significantly lower than in patients without AKI. Additionally, the rate of postoperative AKI development was high in patients with a low rSO₂ and hemoglobin concentration. AKI developed postoperatively in 12 patients, and in patients who developed AKI, rScO₂ levels at 2 and 6 h after CPB were significantly lower than in patients without AKI.

**Conclusion**

Measurement of the rScO₂ and hemoglobin concentration by cerebral oximetry during CABG is considered important for predicting complications associated with high mortality, such as AKI, and taking action against these complications. Moreover, a low rScO₂ can be a determining factor for postoperative AKI, and such patients must therefore be closely monitored for AKI.

In conclusion, monitoring of the rScO₂ and hemoglobin concentration during CABG can be beneficial in terms of estimating perioperative and postoperative complications. The risk of perioperative AKI development in patients with a low rScO₂ and hemoglobin concentration should be considered. Although there is no direct evidence for such a correlation, our study showed that the incidence of AKI was higher in patients with low levels. Therefore, nephrotoxic drugs should be avoided and renal protective measures must be taken. Optimum average blood pressure and hemoglobin levels may have to be reached for this purpose.

**Declaration of conflicting interests**
The authors declare that there is no conflict of interest.

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