# Intraoperative Renal Regional Oxygen Desaturation Can Be a Predictor for Acute Kidney Injury after Cardiac Surgery

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**_Objective:_ To evaluate the usefulness of renal regional oxygen saturation (renal $rSO_2$) in predicting the risk of acute kidney injury (AKI) after cardiac surgery.**

**_Design:_ A prospective observational study.**

**_Setting:_ Tertiary care university hospital.**

**_Participants:_ One hundred patients undergoing cardiac surgery.**

**_Interventions:_ Renal $rSO_2$ was monitored continuously by near-infrared spectroscopy (NIRS) throughout the anesthetic period.**

**_Measurements and Main Results:_ Postoperative AKI was defined using the Risk, Injury, Failure, Loss, and End-stage (RIFLE) criteria. Of 95 patients who were included in the final analysis, 34 patients developed AKI after surgery. Recorded renal $rSO_2$ data were used to calculate the total duration of the time when renal $rSO_2$ was below the threshold values of 70%, 65%, 60%, 55%, and 50%. The total periods when the renal $rSO_2$ level was below each of the threshold values were significantly longer in patients with AKI than in those without AKI ($p = 0.001$ or $p < 0.001$). Receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive power of renal $rSO_2$ for AKI. The ROC curve analysis showed that renal $rSO_2$ could predict the risk of AKI with statistical significance and that a renal $rSO_2 < 55\%$ had the best performance (area under the curve–ROC, 0.777; 95% CI, 0.669-0.885; $p < 0.001$). Multivariate logistic regression analysis revealed that AKI significantly correlated with the duration of renal $rSO_2 < 55\%$ ($p = 0.002$) and logistic EuroSCORE ($p = 0.007$).**

**_Conclusions:_ Intraoperative renal regional oxygen desaturation can be a good predictor of AKI in adult patients undergoing cardiac surgery.**



***KEY WORDS: acute kidney injury, near-infrared spectroscopy, cardiac surgery***

ACUTE KIDNEY INJURY (AKI) is a common and serious complication of cardiac surgery, with a reported incidence as high as 45%.[1,2] It is associated with poor outcomes, prolonged stays in hospital and in an intensive care unit (ICU), and increased mortality.[2,3] Small increases in the levels of serum creatinine (sCr) reflect renal injury and predict poor outcomes.[4] Nevertheless, given that a detectable increase in the levels of sCr does not immediately follow the onset of AKI, sCr levels alone are of limited value for the early identification of the risk of AKI. Biomarkers of early renal injury, such as neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, kidney injury molecule 1, and interleukin (IL)-18, recently have been shown to facilitate earlier diagnosis of AKI.[5,6] Although these biomarkers show some benefits for early detection of AKI, they cannot be measured continuously to monitor renal function in real time, which is needed to optimize the renal condition.

Near-infrared spectroscopy (NIRS) is a new noninvasive technique that continuously monitors regional oxygen saturation ($rSO_2$) by measuring the relative concentrations of oxygenated and deoxygenated hemoglobin within a local tissue area.[7] Previous studies have suggested that low $rSO_2$ values can predict the development of organ dysfunction in the brain or other organs after surgery.[8] Persistent low renal $rSO_2$ has been associated with renal dysfunction after pediatric cardiac surgery.[9] However, to date, the relationship between intraoperative renal $rSO_2$ and AKI in adult patients undergoing cardiac surgery has not been determined.

The authors hypothesized that renal $rSO_2$ measured by NIRS can reflect renal desaturation or hypoxia, which may contribute to AKI. The aim of this study was to examine whether intraoperative renal $rSO_2$ could predict the risk of AKI after cardiac surgery.

## METHODS

After approval by the Institutional Ethics Committee and obtaining written informed consent, a total of 100 adult patients who underwent elective cardiac surgery with cardiopulmonary bypass (CPB) were enrolled between October 2010 and August 2011. Exclusion criteria were off-pump coronary artery bypass surgery (OPCAB), aortic surgery (total arch replacement and/or descending aorta replacement surgery), emergency surgery, left ventricular ejection fraction (LVEF) $< 30\%$, body mass index (BMI) $\geq 30$ kg/m$^2$, sCr $\geq 1.5$ mg/dL, and end-stage renal disease or renal transplant.

Anesthesia was induced with etomidate (0.2 mg/kg), followed by rocuronium (0.8 mg/kg) to facilitate tracheal intubation, and was maintained with a continuous infusion of propofol (1-2 μg/mL) and remifentanil (5-20 ng/mL) using a target-controlled infusion pump (Orchestra Base Primea; Fresenius Kabi, Paris, France). Normal saline and 6% hydroxyethyl starch 130/0.4 (Voluven, Fresenius Kabi, Bad Homburg, Germany) were used for fluid management, and red blood cell (RBC) transfusion was initiated when hemoglobin level was $<8$ g/dL. A 20-G radial arterial catheter was inserted to monitor arterial blood pressure and to allow blood sampling. A 7.5-Fr pulmonary arterial catheter (Swan-Ganz Combo V CCL/$SvO_2$/CEDV; Edwards Lifesciences, Irvine, CA) was advanced and connected to a Vigilance II device (Edwards Lifesciences) to monitor cardiac output and mixed venous oxygen saturation ($SvO_2$). After heparinization (400 U/kg of heparin), CPB was started using a roller pump (Stöckert SIII; Stöckert Instrumente, Munich, Germany), with the tubing system without surface coating (Medtronic, Minneapolis, MN, USA), a membrane oxygenator (Affinity; Medtronic), and a 38-μm blood filter (Medtronic). The CPB flow rate was maintained between 2.2 and 2.5 L/min/m$^2$, and the mean arterial pressure during CPB was maintained at 50 to 80

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mmHg. Alpha-stat pH management was used during CPB. After weaning from CPB, heparin was antagonized by protamine sulfate (4 mg/kg). All patients were transferred to the ICU after surgery, where care was provided by ICU nurses and staff who were not involved in the study in accordance with existing unit protocol. Patients were discharged from the ICU to a general ward when their vital signs were stable and further ICU care and monitoring were not required.

Renal $rSO_2$ was monitored with NIRS (INVOS 5100C; Somanetics Co., Troy, MI) throughout the entire anesthetic period. Before the induction of anesthesia, a disposable NIRS sensor was applied to one or both sides of the flank area that overlies the kidney in order to monitor renal $rSO_2$ under sonographic guidance (Z.one Ultra; ZONARE Medical Systems Inc., Mountain View, CA) (Fig 1). To visualize the kidney, an ultrasound probe was placed in the lower intercostal space (below either the 10th or 11th rib) on the posterior axillary line. After obtaining the long-axis image of the kidney, the renal depth (the distance from the skin surface to the capsule of the kidney) was measured. A sensor then was applied to the probe placement site in instances when the renal depth was $<40$ mm. Patients were excluded from the study if both renal depths were $\geq 40$ mm. Renal $rSO_2$ values were recorded continuously at 5- or 6-second intervals. Whenever renal $rSO_2$ was monitored on both sides, the lower value was selected for analysis. The authors believe that the lower value is clinically more important because selecting the higher value or mean value may mask existing hypoxia, which may contribute to AKI. The sensitivity tests showed that the predictive ability of data including the lower value are better than that of data including the higher or mean value (data not shown). The patient whose monitoring of renal $rSO_2$ was not checked continuously for more than 5 minutes during surgery was excluded from the study. No interventions were attempted based on renal $rSO_2$ values. Cerebral $rSO_2$ also was recorded simultaneously. Recorded $rSO_2$ data were analyzed using Excel software (Microsoft, Seattle, WA). Renal $rSO_2$ data were used to calculate the total duration of renal $rSO_2$ below the threshold value. Multiple thresholds were selected to reflect different degrees of renal hypoxia. The thresholds used were renal $rSO_2$ values of 70%, 65%, 60%, 55%, and 50%. These represent the approximate mean value of the baseline ($80.0 \pm 9.1\%$) minus 1, 1.5, 2, 2.5, and 3 standard deviations (SDs), respectively. In addition, the other thresholds used were the proportionate decline form baseline value (10%, 15%, 20%, 25%, and 30%).

Demographic data included age, sex, BMI, diabetes mellitus, hypertension, peripheral vascular disease, LVEF, logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation), renal depth, baseline renal $rSO_2$, preoperative hemoglobin, preoperative sCr, and preoperative estimated glomerular filtration rate (eGFR). The eGFR was calculated using the modification of diet in the renal disease (MDRD) formula [$\text{eGFR} = 186 \times \text{creatinine}^{-1.154} \times \text{age}^{-0.203} \times 0.742$ (if female)].[10] Intraoperative variables included the type of surgery, surgical time, CPB time, fluid infusion volume (crystalloid and colloid), urine output, number of patients requiring blood transfusion, and intraoperative minimum hemoglobin. The intraoperative vital signs (heart rate, mean arterial pressure, central venous pressure, mean pulmonary arterial pressure, cardiac index, and $SvO_2$) and arterial blood gas analysis data (arterial oxygen pressure, hemoglobin, and lactate) were recorded after induction, before CPB, after CPB, and at the end of surgery.

The primary outcome was the development of AKI, which was defined as an absolute increase in sCr by $\geq 50\%$ or a decrease in eGFR by $\geq 25\%$ from the preoperative baseline within 5 days after surgery, according to the Risk, Injury, Failure, Loss, and End-stage (RIFLE) criteria.[11] Postoperative sCr was recorded daily for 5 days after surgery when available, and the highest value was used for analysis. Renal replacement therapy (RRT) was started using continuous venovenous hemodialysis when life-threatening conditions such as severe fluid, electrolyte, and acid-base imbalance could not be managed by conservative treatment. The secondary outcomes included time to discharge from the ICU and hospital, RRT, and in-hospital mortality.

Data are presented as the means $\pm$ SDs, medians (interquartile range), or numbers of patients (%). Statistical analyses were performed using SPSS for Windows version 18.0 (SPSS Inc., Chicago, IL). Continuous variables were compared using the independent Student's *t* test or Mann-Whitney U test. Categoric variables were analyzed using the chi-square test or Fisher's exact test. To compare the changes in cerebral and renal $rSO_2$ tracing using a linear mixed effect model, the lowest values of $rSO_2$ during every minute were selected (i) from 5 minutes before induction until 55 minutes after induction, (ii) from 20 minutes before CPB until 60 minutes after CPB on, and (iii) from 60 minutes before CPB off to 100 minutes after CPB off. The same method was used to compare changes in renal $rSO_2$ tracing between patients with AKI and those without AKI. To determine the predictive power and the best predictive threshold value of renal $rSO_2$ for AKI, receiver operating characteristic (ROC) curve analysis was performed at multiple threshold values of renal $rSO_2$. To calculate the statistical power (1–β) of the ROC curve analysis, power analysis was tested using PASS 11 (NCSS Statistical Software Co., Kaysville, Utah); null hypothesis is that renal $rSO_2$ cannot predict the risk of AKI [area under the curve (AUC)–ROC is 0.5], and the number of positive groups (patients with AKI) and negative groups (patients without AKI), α (p value), and AUC-ROC that were evaluated in the ROC curve analysis were used. The relationship among renal $rSO_2$ and the intraoperative vital sign and arterial blood gas analysis variables at each time point was determined using a linear regression analysis. Initially, all covariates (heart rate, mean arterial pressure, central venous pressure, mean pulmonary arterial pressure, cardiac index, $SvO_2$, arterial oxygen pressure, hemoglobin, and lactate) were evaluated independently and were candidates for the multivariate linear regression model. A stepwise backward elimination process was used to develop the

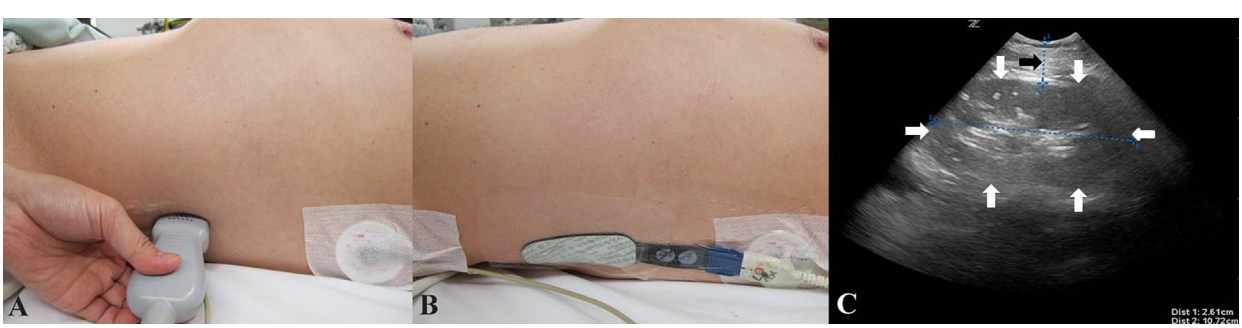


**Fig 1. The application of an NIRS sensor to the flank that lies above the kidney. (A) The location of the kidney was checked by sonography. (B) A NIRS sensor was applied to the probe placement site. (C) Sonographic findings for the long-axis image of the kidney. White arrows indicate the outline of the kidney. Black arrow indicates the measurement line of renal depth. NIRS, near-infrared spectroscopy.**