Faculté de pharmacie et des
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Association between end of surgery cerebral tissue oxygen saturation as measured by cerebral near-infrared spectroscopy and the incidence of acute kidney injury after cardiac surgery

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Abstract

English

Acute kidney injury (AKI) is linked to multiple morbidities and an increased mortality rate. It is a common cardiac surgery-related complication. Early diagnosis could limit the progression of AKI, but current screening techniques are still limiting. However, new studies are focusing on the application of near-infrared spectroscopy (NIRS). The device is connected to electrodes that are placed on the skin to measure the regional oxygen saturation (rSO_2). This study investigates an association between NIRS measurements of the brain's regional oxygen saturation at the end of cardiac surgery and the onset of cardiac surgery-related acute kidney injury (CSR-AKI).

The data for this retrospective study was taken from 2020 patients undergoing cardiac surgery at the Cliniques Universitaires Saint-Luc between 2006 and 2019. Following the criteria of the Acute Kidney Injury Network (AKIN) classification, 10.6% (210) of the patients were classified as having developed CSR-AKI. Multiple variables were compared, including mean preoperative and postoperative cerebral rSO_2, the most determining variable in this study. In addition, a second study was carried out among patients who presented cerebral desaturation during the operation of at least 20%. Lastly, a multivariate analysis was performed to look at the effect of the measurements taken by NIRS in a more comprehensive model.

The cerebral rSO_2 ($rScO_2$) of 2020 patients was measured throughout cardiac surgery using an INVOS^{TM} cerebral NIRS. The average postoperative cerebral rSO_2 was associated with a lower measure in patients who developed CSR-AKI than in patients who did not. The other variables also showed a significant odds ratio except for sex, body mass index (BMI), maximum area under the curve (AUC) and maximum suppression ratio (SR). Comparable results were observed in the group of patients with cerebral desaturation during the operation of at least 20%. In the multivariate analysis, the postoperative $rScO_2$ taken by NIRS was significant.

Measurements of $rScO_2$ by the NIRS at the end of cardiac surgery have the potential to help physicians predict the onset of CSR-AKI. However, its exact relationship between regional cerebral oxygen saturation and the occurrence of AKI requires further studies.

French

L’insuffisance rénale aiguë (IRA) est liées à de multiples comorbidités et à un taux de mortalité accru. Elle est une complication fréquente de la chirurgie cardiaque. Une détection précoce permettrait de prévenir la dysfonction rénale et d’améliorer la prise en charge de l’IRA post opératoire (PO), mais les techniques de dépistage actuelles sont encore limitées. Cependant, de nouvelles études se penchent sur l’utilisation de la spectroscopie proche infrarouge (SPIR). Le dispositif est connecté à des électrodes qui sont placées sur la peau pour mesurer la saturation régionale en oxygène (rSO_2). Dans le cadre de cette étude, les électrodes étaient placées sur le front des patients afin d’interroger l’association entre les valeurs de rSO_2 cérébrale mesurée par une SPIR à la fin de l’intervention cardiaque et l'apparition d’insuffisance rénale aiguë en post-opératoire (IRA-PO).

Les données de cette étude rétrospective proviennent de 2020 patients ayant subi une chirurgie cardiaque aux Cliniques Universitaires Saint-Luc entre 2006 et 2019. En suivant les critères de l’échelle Acute Kidney Injury Network (AKIN), 10.6% (210) patients ont été classés comme ayant développé une CSR-AKI. De multiples variables ont été comparées dont la rSO_2 cérébral moyenne préopératoire et postopératoire, la variable la plus déterminante de cette étude. En outre, une deuxième étude a été réalisée parmi les patients ayant présenté une désaturation cérébrale pendant l'opération d’au moins 20 %. Pour terminer, une analyse multivarié a été construit pour regarder l’effet des mesures prises par la SPIR dans un modèle plus complet.

A l'aide d'une SPIR cérébrale INVOS^{TM}, les rSO_2 cérébraux ($rScO_2$) de 2020 patients ont été mesurées tout au long l’intervention chirurgicale. La $rScO_2$ moyenne postopératoire était associée à une cote plus faible chez les patients ayant développé une IRA-PO comparativement aux des patients n'en ayant pas développée. Les autres variables ont également montré un rapport de cote significatif à l'exception des variables sexe, indice de masse corporelle (IMC), l’aire sous la courbe (AUC) maximale, et la suppression ratio (SR) maximale. Des résultats comparables ont été observés dans le groupe de patients présentant une désaturation cérébrale pendant l'opération d’au moins 20%. Dans le modèle multivarié, la $rScO_2$ postopératoire mesurée par SPIR est significative.

Les mesures de la $rScO_2$ par SPIR à la fin d'une chirurgie cardiaque pourraient aider les médecins à prédire l'apparition d'une IRA-PO. Cependant, la relation exacte entre la saturation régionale d’oxygène cérébrale et la mauvaise évolution rénale nécessite des études ultérieures.

Introduction

Acute Kidney Injury: Definition and pathology

Acute Kidney Injury (AKI) is characterized by a rapid loss of the kidney's function. The term "Acute Kidney Injury" has replaced the term "Acute Renal Failure" (ARF) in order to better express the variability and evolution of kidney dysfunction. Kidney dysfunction can evolve quickly and can cause complications involving other organs that, in turn, will negatively affect the kidney (Grams and Rabb 2012). Therefore, it is important to understand AKI and its different stages in order to better treat patients and minimize its progression.

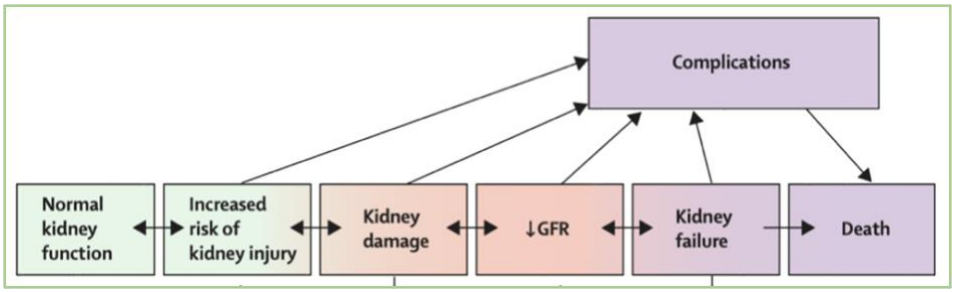

Figure 1: Evolution of acute kidney injury. Complications can appear from any stages of kidney dysfunction, and aggravate the consequences (Bellomo, Kellum, and Ronco 2012).

AKI can be caused by many factors but is usually due to a decrease in the delivery of blood to the kidney, or ischemia (Olivero et al. 2012). When the blood pressure drops, the issue is picked up by the Renin-Angiotensin-Aldosterone System (RAAS). This system will cause respond by causing the constriction of arterioles, an increased heart rate, an increased absorption of sodium, and an increased excretion of potassium and water retention. All of these mechanisms will increase the blood's pressure and help the body return to homeostasis (Wallace 1998; Patel et al. 2017). When RAAS is activated for too long, the endothelial cells in the kidneys can be damaged, along with the overall vessels, leading to inflammation, renal hypoxia, and oxidative stress. Thickening and fibrosis of the renal tissues may arise due to the damaged vessels (Olivero et al. 2012) and aggravate the kidneys' malfunction.

Due to the strain of cardiac surgery, patients are at a much higher risk of developing AKI. According to Bhat et al. (1976); Choi et al. (2014); Graziani et al. (2019), 35 to 45% of adults developed AKI following cardiac surgery. Cardiac surgery-related AKI (CSR-AKI) has been associated with poor outcomes, such as a longer stay in hospital and in ICU, along with a mortality rate that can reach up to 80% (Olivero et al. 2012). It is the second most common

type of AKI in the intensive care setting (Wang and Bellomo 2017), and leads to higher in-hospital mortality rates compared to patients without AKI (Mao et al. 2013).

Acute Kidney Injury Network (AKIN)

The Acute Kidney Injury Network (AKIN) is a model created to assess the presence and degree of kidney injury by following changes in a patient's urine output and serum creatinine concentrations (Figure 2). This helps physicians diagnose and classify their patients easily and improve treatment and monitoring (Mehta et al. 2007).

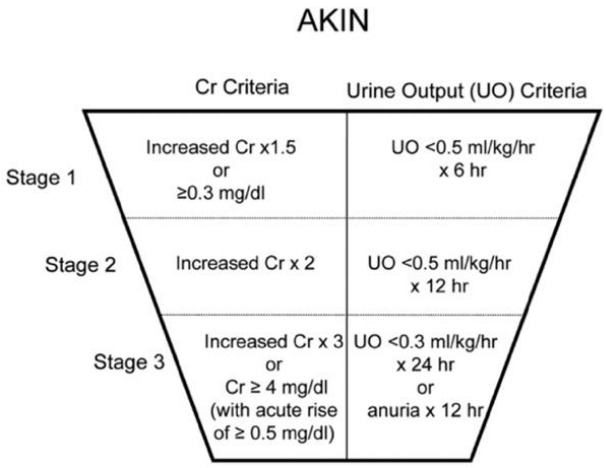

Figure 2: AKIN stages based on serum creatinine concentrations and urine output. Serum creatinine concentration is looked at as an increase by fold or an increase in concentration. Urine output is looked at in terms of quantity over a given period (Cruz, Ricci, and Ronco 2009).

Current diagnosis methods

The most common screening method for CSR-AKI is to follow at the patient's urine output and creatinine concentration (Bellomo, Kellum, and Ronco 2012). Creatinine is continuously produced by muscles and excreted into the urine by the kidneys. The volume of urine filtered by the kidney over time is represented by the glomerular filtration rate (GFR). The GFR describes the kidney's ability to filter plasma through the glomerulus, a complex of capillaries allowing the transfer of smaller particles. It is important to understand that GFR depends largely on the age and muscular mass of the patient. A correlation exists between serum level of creatinine, age, weight and creatine clearance allowing to estimate GFR (Ronco, Bellomo, and Kellum 2017). When the GFR is affected, the kidneys are less able to separate molecules in the plasma, and less urine will be produced. Creatinine will therefore accumulate in the serum instead of being excreted, and its level can be seen through a blood test.

While serum creatinine levels and urine output can easily be measured, they do not always change when the GFR is lowered. An increased serum creatinine concentration and dropped urine output are associated with reduced kidney function, but they only appear when the kidney is already severely affected. Serum creatinine levels tend to remain relatively normal until approximately 50% of the nephrons are lost or if the GFR approaches 60 mL/min/1.73m^2, and these values drop with an increasing age (normal GFR: 90 - 120 mL/min/1.73m^2 in men under 40 years old, 75 for men overs 70 years old, Ronco, Bellomo, and Kellum (2017)). They do not allow for early detection of AKI or to halt its progression.

To help detect the onset of CSR-AKI as soon as possible, some renal biomarkers have been analyzed. Compared to urine output and creatinine concentration, they require less monitoring time and could detect injuries earlier (Hazle et al. 2013). Some biomarkers have helped increase CSR-AKI prediction risk or determine the therapy needed, yet they can only be used when the injury has already developed. In addition, they are not conclusive enough to be used without a clinical assessment or a model (Wang and Bellomo 2017). Urine output and serum creatinine concentration remains the standard for detecting CSR-AKI.

Near-Infrared Spectroscopy (NIRS)-based oximeter

Recent studies have turned to the potential use of near-infrared spectroscopy (NIRS) to detect CSR-AKI. The NIRS-based oximeter can measure oxygen levels in both arteries and veins. This allows physicians to determine whether enough oxygen is brought to the tissues to perfuse the organ normally. Arterial oximeters only consider arteries and therefore the oxygen being brought into the tissues. This difference between these two techniques is crucial to identifying hypoxia during cardiac surgery. When hypoxia occurs, the oxygen saturation in both veins and arteries drops. The NIRS will detect the drop in both compartments, but with an arterial oximeter, this change will be detected later and delay a response, allowing the condition to worsen (Cheung et al. 2022).

The NIRS-based oximeter is routinely used during cardiac surgery to monitor the patient's regional cerebral oxygen saturation ($rScO_2$) and allow an intervention in cases of major saturation drops. The brain is a high oxygen-consuming organ therefore, researchers have suggested that monitoring $rScO_2$ could improve oxygenation and perfusion pressure in other tissues (Balci, Haftaci, and Kunt 2018), such as the kidneys.

The NIRS-based tissue oximeter is an easy and non-invasive technique that can be applied to adults, children, and infants. The electrodes are placed directly on the forehead,

where they will read the frontal lobes' oxygen balance. Therefore, a drop in the kidneys' regional oxygen saturation (rSO_2) could be suspected and help diagnose the early stages of its malfunction (Owens et al. 2011). In children undergoing cardiac surgery, electrodes can be directly placed on the backside to measure the kidneys' rSO_2, but this is not possible in adults. Kidneys in adults lie under a lot of tissue, and the wavelengths produced by the NIRS are not strong enough to reach renal tissues (Choi et al. 2014). The frontal lobes, on the other hand, have a much thinner layer of tissues between the electrodes and the brain, allowing a proper reading. Even if studies have proven that cerebral oximetry does not allow for a prediction as strong as renal oximetry (Owens et al. 2011), this method is not applicable to adult patients.

NIRS-based oximeter's mechanism

Patients' cerebral oxygen saturation will be measured through an NIRS-based cerebral oximeter. This device is connected to electrodes that are placed directly on the forehead's skin and emit wavelengths of near-infrared light (700 and 850 nanometers) into cerebral tissues. The wavelengths emitted travel through the tissues in a semi-circular path and back to two detectors. The shallow and deep detectors, respectively, are placed 3 cm and 4 cm away from the light source and measure the superficial and deep tissues to remove variations due to extra-cerebral tissues (Figure 3). The oximeter can assess the amount of oxygenated and unoxygenated content in the tissues and thus calculate the regional tissue oxygenation saturation (Francoeur et al. 2022).

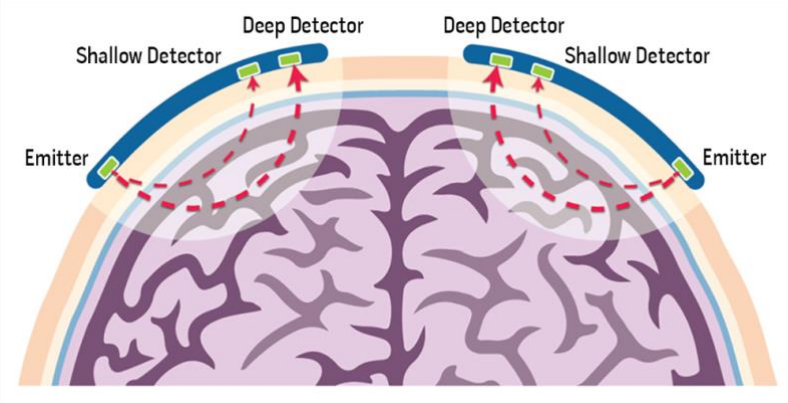

Figure 3. INVOS^{TM} cerebral oximeter electrodes and the wavelengths emitted through superficial and deep tissues. From "INVOS^{TM} Near Infra-Red Spectroscopy" (Polderman 2019).

The oximeter's electrodes emit wavelengths specific to oxygen-bound and unbound hemoglobin (Hb) and the reflection can be detected. This difference is described by the Law

of Beer-Lambert. Hemoglobin, however, is not the only factor that will absorb photons in the near-infrared; melanin, bilirubin, and water also play a role (Figure 4). To counter the effect of melanin, the electrodes simply must emit their wavelengths beyond 100 µm to avoid any attenuation of the signal. The influence of bilirubin is slightly more complicated. If the patient has any signs of jaundice, it will affect the oximeter's measurement. The best way to avoid its effects is to establish for each patient a baseline value at the beginning of the procedure and observe changes from this value rather than an assumed set point for all patients (Murkin and Arango 2009). This also allows for control over the effects of water. Otherwise, the NIRS-based oximeter monitors that use five wavelengths of infrared can attenuate the effect of bilirubin (Magasich-Airola et al. 2022).

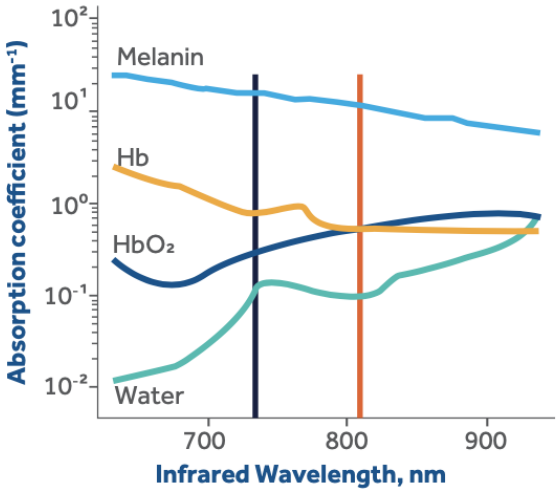

Figure 4: Photon absorption in the cranium. Melanin and water are the main competing infrared absorbers and may influence measurements by the NIRS-based oximeter. Unoxygenated hemoglobin absorbs best at shorter wavelengths (Edmonds 2018). Hb = unoxygenated hemoglobin; HbO_2 = oxygenated hemoglobin.

Regional oxygen saturation over time

The oximeter measured the patient's $rScO_2$ throughout the procedure and assessed any decrease from their baseline value. From these continuous measurements, a graph looking at the patient's $rScO_2$ throughout time can be traced, and a measure of the area under the curve (AUC) can be drawn. An example looking at tissue oxygen saturation (StO_2) can be seen in Figure 5. A high AUC translates to either a high desaturation rate over a period of time or a desaturation over prolonged of time. It is measured in percentage-minute.

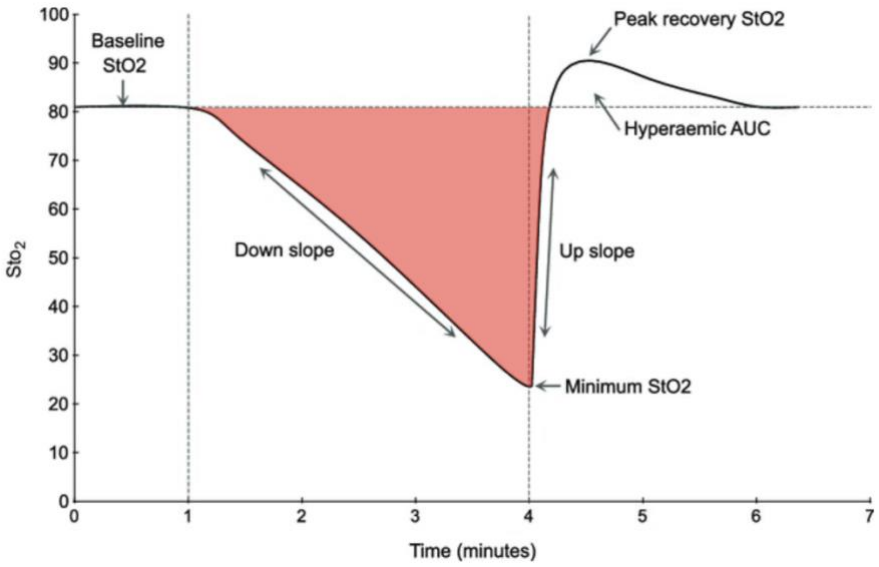

Figure 5. Example of tissue SO_2 (StO_2) throughout time generated by a NIRS vascular occlusion test. The highlighted zone represents the patient's desaturation, or AUC. AUC = area under the curve; StO2 = tissue oxygen saturation (Martin et al. 2013).

Hypothesis

This study hypothesizes that patients in whom the postoperative cerebral rSO_2 was in a lower range were at higher risk of cardiac surgery-related AKI (CSR-AKI). This is investigated by studying the association between intraoperative cerebral NIRS measurements (INVOS^{TM}) taken at the end of cardiac surgery and the onset of CSR-AKI as determined by the AKIN model.

Methods and Materials

Patient Sample

The study is retrospective and includes patients who underwent cardiac surgery at the Cliniques Universitaires Saint-Luc (CUSL) between 2006 and 2019. Some of the patients required an aorta clamping or a bypass during their surgery. The patients were exclusively recruited from the cardiac department only.

Data collection

Clinical data was extracted from the CUSL's medical records. Two datasheets were combined and refined to contain the following variables: gender, age, weight, height, preoperative and multiple postoperative creatinine concentrations, preoperative and postoperative $rScO_2$ measurements from the left and right side of the brain, a calculated European System for Cardiac Operative Risk Evaluation II (EuroSCORE II), preoperative and postoperative hemoglobin concentrations during cardiac surgery, length of stay in intensive care unit (ICU) and hospital, mortality, maximum area under the curve (AUC) of the $rScO_2$ recorded during cardiac surgery, maximum suppression ratio (SR) recorded during cardiac surgery, and the duration of cardiopulmonary bypass (CPB) and aorta clamping (AoC) during cardiac surgery. EuroSCORE II is a logistic regression model based on the patient's clinical measurements and existing conditions used to determine a patient's mortality risk after cardiac surgery. From this data, the average $rScO_2$ before and after surgery were calculated, as were the maximum creatinine concentration and body mass index (BMI).

Acute Kidney Injury Network (AKIN)

The concentration of creatinine in the serum was measured before and after surgery. This is done by a simple blood test, and the serum concentration is measured in mg/dL. Data was collected first before surgery and then each day for one week following the surgery. Once the data is collected for each patient, the maximal post-operative concentration is compared to the pre-operative concentration as a percentage difference and as an increase or decrease value in mg/dL.

Each patient from the database was classified into no stage (no AKI), stage 1, stage 2, or stage 3 based on the creatinine levels measured before and after surgery. If a patient can be

categorized into 2 stages according to AKIN, for example, with a 2-fold increase (stage 2 AKI) but a concentration higher than 4 mg/dL with an increase of 2.5 mg/dL (stage 3 AKI), the patient is classified as the highest stage, in this case stage 3. This classification allows the study to have a clear separation between patients with and without AKI in order to analyze the differences and similarities between the two groups. The classification of patients is summarized in Table 1.

Statistical analysis

Patients with missing data were excluded from the study. Patients' preoperative and postoperative measurements were assessed according to the AKIN classification. Categorical variables are presented as a number (%) while continuous variables are presented as a median (interquartile range). To compare the AKI and non-AKI patients, the normality of each variable was verified using a Shapiro-Wilk test. If the variable was normally distributed, an independent t-test was used. Otherwise, a non-parametric test was used: the Mann-Whitney test for continuous variables and the chi-squared test for a dichotomous variable. These tests were run with the software SPSS^{TM}, with a significance level of 0.05 for the p-value.

Possible predictors of CSR-AKI were analyzed using odds ratios to find associations between our variables and the onset of CSR-AKI. The variables were tested individually between the two groups, with statistical significance measured by a 95% confidence interval.

A similar analysis was made using only patients who had shown a cerebral desaturation of 20% or more from their baseline value. Odds ratios were calculated for various preoperative and postoperative variables. The statistical significance was measured by a 95% confidence interval.

Lastly, outcomes were assessed using a multivariate model. Variables were examined through a logistic regression. The first model contains only the variable mean $rScO_2$ postoperative. The second model contains variables that did not have any collinearity with the variables mean postoperative $rScO_2$ and showed a significant odds ratio in the previous tests. The last model contains variables that did not have any collinearity with the variable mean postoperative $rScO_2$, regardless of their previously calculated odds ratio. Collinearity was determined with the variance inflation factor (VIF) with an exclusion setpoint of 3. A likelihood-ratio test was assessed to determine the better-fitting model at a level of significance of 95%. The odds ratios' statistical significance in the models was measured by a 95% confidence interval.

Results

Patient classification by AKIN

2,024 patients were classified through the AKIN model. 4 patients were excluded from the study due to missing data. 1,810 patients were classified in stage 0, 147 patients in stage 1, 32 patients in stage 2, and 31 patients in stage 3 (Table 1). For the rest of this study, patients are separated into two groups: AKI and non-AKI, with 210 and 1,810 patients, respectively.

Table 1. Description of the patients classified by AKIN

	Number of Patients (N)	**Percentage of Patients (%)**
Stage 0	1,810	89.4
Stage 1	147	7.3
Stage 2	32	1.6
Stage 3	31	1.5
Total	2,020	99.8
Missing Data	4	0.2
Total	**2,024**	**100.0**

Preoperative characteristics of patient with CSR-AKI

A total of 2,020 patients had their cerebral oxygen saturation measured throughout surgery. Among these patients, the mean age was 66.7 years old, 71.6% male, with a mean BMI of 30.1. Patients with CSR-AKI were older and had a higher BMI compared to non-AKI patients. The median serum creatinine concentration was higher in patients with CSR-AKI. The oximeter measured a lower $rScO_2$ on both frontal lobes in patients with CSR-AKI (58.0% and 60% on the left and right sides for AKI patients, and 63.0% on each side for non-AKI patients). The mean preoperative $rScO_2$ was also lower in patients with AKI (59.0%) compared to non-AKI patients (63.0%). The EuroSCORE II was more than doubled in patients with CSR-

AKI. They also had a lower hemoglobin concentration compared to patients without CSR-AKI (Table 2).

Table 2. Preoperative clinical characteristics of patients classified by AKIN

Characteristics	**AKI (N = 210)** Median (IQR)	**No AKI (N = 1810)** Median (IQR)	**p-value**
Demographic			
Male (number)	153 (72.9 %)	1,293 (71.4 %)	0.666
Age (year)	70 (63 – 79)	68 (60 - 75)	0.006
BMI (kg/m^2)	27.4 (24.4 – 30.8)	26.6 (24.0 – 30.1)	0.040
Serum creatinine (mg/dL)			
Preoperative	1.14 (0.92 – 1.56)	0.96 (0.83 – 1.13)	<0.001
Preoperative rScO$_2$ (%)			
Average *	59.0 (50.8 – 66.5)	63.0 (57.0 – 69.0)	<0.001
Left frontal lobe	58.0 (50.0 – 65.8)	63.0 (56.0 - 69.0)	<0.001
Right frontal lobe	60.0 (51.0 – 66.0)	63.0 (57.0 – 69.0)	<0.001
EuroSCORE II (%) §	3.88 (2.00 – 7.75)	1.98 (1.08 – 3.48)	<0.001
Hemoglobin concentration (g/dL)			
Preoperative	12.8 (11.3 – 14.5)	13.9 (12.8 – 15.0)	<0.001

AKI = acute kidney injury; IQR = interquartile range; BMI = body mass index; rScO$_2$ = regional cerebral oxygen saturation.
* The patients' rScO$_2$ was measured from electrodes on the left and right frontal lobes. The average between the two was calculated and used for statistical analysis.
§ EuroSCORE II predicts the risk of mortality for patients undergoing cardiac surgery. It is calculated based on 18 different criteria, each associated with an added percentage risk. The score is a percentage. A higher score indicates a higher risk of mortality when undergoing cardiac surgery.

Postoperative characteristics of patients with CSR-AKI

A total of 2,020 patients had parameters measured throughout cardiac surgery and at the end. The maximum serum creatinine concentration was more than doubled in patients with AKI. The median rScO$_2$ during the closing of the thorax skin was lower on the left (60.0%) and right (61.0%) front lobes, as well as the average of the two sides (60.5%), in patients with AKI than in patients with no AKI (64.0%, 65.0%, 64.5%). Patients with AKI had a median stay in the ICU that doubled compared to non-AKI patients and a higher hospital stay. The mortality rate in patients with AKI was much higher than in patients with no AKI (15.7% vs. 2.0%). The maximum AUC showed the same median but very different interquartile ranges.

The maximum SR was higher in patients with AKI. Hemoglobin concentrations after the surgery were higher in patients with no AKI. Lastly, the duration of the cardiopulmonary bypass and the aorta clamping were both increased in patients who developed AKI (Table 3).

Table 3. Postoperative clinical characteristics of patients classified by AKIN

Characteristics	**AKI (N = 210)** Median (IQR)	**No AKI (N = 1810)** Median (IQR)	**p-value**
Serum creatinine (mg/dL)			
Maximum *	1.89 (1.49 – 2.70)	0.91 (0.77 – 1.07)	<0.001
$rScO_2$ at closing of the skin (%)			
Average §	60.5 (55.5 – 68.5)	64.5 (59.0 – 71.3)	<0.001
Left frontal lobe	60.0 (55.0 – 68.0)	64.0 (58.0 – 71.0)	<0.001
Right frontal lobe	61.0 (55.0 – 69.0)	65.0 (59.0 – 72.0)	<0.001
Stay (days)			
ICU	4 (2 – 7)	2 (2 – 3)	<0.001
Hospital	11 (8 – 18)	8 (7 – 10)	<0.001
Death	33 (15.7 %)	36 (2.0 %)	<0.001
Maximum AUC (%min) †	0 (0 – 14.5)	0 (0 – 3)	0.040
Maximum SR (min) ‡	2.2 (0 – 12.2)	1.3 (0 – 9.55)	0.022
Hemoglobin concentration (g/dL)			
Postoperative	9.2 (8.7 – 10.0)	9.9 (9.0 – 10.9)	<0.001
CPB duration (min)	110.5 (87.5 – 152.0)	103.0 (77.0 – 133.5)	<0.001
Aorta clamping duration (min)	78.0 (62.5 – 116.5)	77.0 (55.0 – 102.0)	0.027

AKI = acute kidney injury; IQR = interquartile range; $rScO_2$ = regional cerebral oxygen saturation; ICU = intensive care unit; AUC = area under the curve; SR = suppression ratio; CPB = cardiopulmonary bypass.

* Seven daily measurements were taken following the surgery. The highest serum creatinine concentration was retained. If data from any days was missing, the highest was taken from the available measurements.

§ The patients' $rScO_2$ was measured from electrodes on the left and right frontal lobes. The average between the two was calculated and used for statistical analysis.

† The area under the curve for the patients' $rScO_2$ was measured from measurements of the left and right frontal lobes. The maximum between the two was used for the statistical analysis.

‡ The suppression ratio values were measured on the left and right frontal lobes. The maximum value was used for the statistical analysis.

Preoperative factors and the onset of CSR-AKI

Unadjusted odds ratios are shown in Table 4 for various measurements taken before or at the beginning of the surgery. An advanced age, both higher preoperative serum creatinine and EuroSCORE II were associated with higher odds of CSR-AKI. On the other hand, a lower mean preoperative $rScO_2$ (odds ratio, 0.957; 95% confidence interval [CI], 0.944 to 0.970) and lower preoperative hemoglobin concentration were associated with higher odds of CSR-AKI. Gender and BMI did not show any association with the development of CSR-AKI.

Table 4. Unadjusted odds ratio of preoperative measures for the onset of CSR-AKI

Variable	Odds Ratio	95% CI for OR
Demographic		
Male	0.932	0.676 – 1.284
Age	1.017	1.005 – 1.029
BMI	0.999	0.996 – 1.003
Creatinine concentration		
Preoperative	1.556	1.331 – 1.818
Mean $rScO_2$		
Preoperative *	0.957	0.944 – 0.970
EuroSCORE II §	1.083	1.058 – 1.108
Hemoglobin concentration		
Preoperative	0.776	0.723 – 0.832

CSR-AKI = cardiac surgery-related acute kidney injury; BMI = body mass index; rScO2 = regional cerebral oxygen saturation; CI = confidence interval; OR = odds ratio.

* The patients' $rScO_2$ was measured from electrodes on the left and right frontal lobes. The average between the two was calculated and used for statistical analysis.

§ EuroSCORE II predicts the risk of mortality for patients undergoing cardiac surgery. It is calculated based on 18 different criteria, each associated with an added percentage risk. The score is a percentage. A higher score indicates a higher risk of mortality when undergoing cardiac surgery.

Postoperative factors and the onset of CSR-AKI

Unadjusted odds ratios are shown in Table 5 for measurements taken during or after surgery. An increased maximum serum creatinine concentration, ICU stay, hospital stay, duration of the cardiopulmonary bypass, and aortic clamping were associated with higher odds

of CSR-AKI. Mortality was associated with CSR-AKI. On the other hand, both decrease in mean postoperative $rScO_2$ (odds ratio: 0.968; 95% CI: 0.948 to 0.977) and hemoglobin measurements were associated with higher odds of developing CSR-AKI. The maximum AUC and SR did not show any association with the development of CSR-AKI.

Table 5. Unadjusted odds ratio of postoperative measures for the onset of CSR-AKI

Variable	Odds Ratio	95% CI for OR
Creatinine concentration		
Maximum *	6.543	4.965 – 8.621
Mean $rScO_2$		
At closing of the skin §	0.968	0.948 – 0.977
Stay		
ICU	1.088	1.056 – 1.120
Hospital	1.011	1.003 – 1.019
Death	9.187	5.589 – 15.102
Maximum AUC †	1.001	1.000 – 1.002
Maximum SR ‡	1.004	0.998 – 1.011
Hemoglobin concentration		
Postoperative	0.750	0.672 – 0.837
CPB duration	1.007	1.005 – 1.101
Aorta clamping duration	1.006	1.003 – 1.010

CSR-AKI = cardiac surgery-related acute kidney injury; $rScO_2$ = cerebral oxygen saturation; ICU = intensive care unit; AUC = area under the curve; SR = suppression ratio; CPB = cardiopulmonary bypass; CI = confidence interval; OR = odds ratio.

* Seven daily measurements were taken following the surgery. The highest serum creatinine concentration was retained. If data from any days was missing, the highest was taken from the available measurements.

§ The patients' $rScO_2$ was measured from electrodes on the left and right frontal lobes. The average between the two was calculated and used for statistical analysis.

† The area under the curve for the patients' $rScO_2$ was measured from measurements of the left and right frontal lobes. The maximum between the two was used for the statistical analysis.

‡ The suppression ratio values were measured on the left and right frontal lobes. The maximum value was used for the statistical analysis.

Outcomes of patients with severe cerebral desaturation of 20% or more

A total of 55 patients were analyzed and classified according to the AKIN model, with 9 patients having developed CSR-AKI and 46 had not, as shown in Table 6. The preoperative serum creatinine concentration was lower in patients with AKI, while their maximum postoperative serum creatinine concentration was higher compared to non-AKI patients. The maximum AUC and SR were both increased in patients with AKI. The NIRS-based oximeter's measurements showed a lower $rScO_2$ in patients who developed AKI on the left and right frontal lobes, both before and at the end of surgery. The mean preoperative and postoperative $rScO_2$ were also lower in patients with AKI (63.8%; 47.5%) compared to non-AKI patients (69.6%; 52.0%).

Table 6. Clinical characteristics for patients classified by AKIN among patients showing severe cerebral desaturation

Variable	**AKI (n = 9)** Median (IQR)	**No AKI (n = 46)** Median (IQR)	**p-value**
Creatinine concentrations (mg/dL)			
Preoperative	0.91 (0.79 – 1.03)	0.99 (0.85 – 1.11)	0.670
Maximum postoperative *	1.58 (1.27 – 2.12)	0.92 (0.79 – 1.06)	<0.001
Maximum AUC (%min) §	76.0 (9.0 – 605.5)	73.5 (2.8 – 198.5)	0.550
Maximum SR (min) †	2.5 (0.3 – 9.5)	1.4 (0.0 – 14.5)	0.796
rScO2 (%)			
Preoperative left frontal lobe	59.0 (49.3 – 67.5)	71.0 (63.8 – 75.3)	0.007
At closing of the skin left frontal lobe	45.0 (37.5 – 51.8)	53.0 (47.0 – 61.3)	0.020
Preoperative right frontal lobe	61.00 (51.8 – 71.8)	70.0 (62.3 – 76.0)	0.048
At closing of the skin right frontal lobe	48.5 (33.5 – 52.3)	53.5 (43.5 – 58.0)	0.026
Mean rScO2 (%) ‡			
Preoperative	63.8 (49.0 – 69.5)	69.6 (64.4 – 76.1)	0.025
At closing of the skin	47.5 (35.5 – 52.0)	52.0 (45.6 – 59.5)	0.031

AKI = acute kidney injury; AUC = area under the curve; SR = suppression ratio; RScO2 = cerebral oxygen saturation.

* Seven daily measurements were taken following the surgery. The highest serum creatinine concentration was retained. If data from any days was missing, the highest was taken from the available measurements.

§ The area under the curve for the patients' RScO2 was measured from measurements of the left and right frontal lobes. The maximum between the two was used for the statistical analysis.

† The suppression ratio values were measured on the left and right frontal lobes. The maximum value was used for the statistical analysis

‡ The patients' $rScO_2$ was measured from electrodes on the left and right frontal lobes. The average between the two was calculated and used for statistical analysis.

Adjusted odds ratio for the onset of CSR-AKI

A model with the unadjusted and adjusted odds ratio of the development of CSR-AKI is presented in Table 7. Model 1 contains the unadjusted odds ratio for our variable of interest, mean $rScO_2$ measured after cardiac surgery to the development of CSR-AKI, and showing a significant association to CSR-AKI when mean $rScO_2$ is lowered (odds ratio, 0.964; 95% CI = 0.950 to 0.978). Model 2 contains the all variables but those with a collinearity to mean postoperative $rScO_2$ and variables showing non-significant odds ratio in Table 4 and 5. This model does not demonstrate a significant association between mean postoperative $rScO_2$ and CSR-AKI (odds ratio, 0.983; 95% CI, 0.966 to 1.001). Model 3 contains variables with no collinearity to mean postoperative $rScO_2$ regardless of their previous odd ratio. In this model, an increased mean postoperative $rScO_2$ is associated with a lowered odds of CSR-AKI (odds ratio = 0.982; 95% CI = 0.964 to 0.999).

Table 7. Unadjusted and adjusted odds ratios for the onset of CSR-AKI

Variable	Model 1	Model 2	Model 3
	Odds ratio (95% IC)		
Mean $rScO_2$ †			
Postoperative	0.968 (0.948 – 0.977)	0.983 (0.966 – 1.001)	0.982 (0.964 – 0.999)
Age		1.014 (1.001 – 1.028)	1.016 (1.002 – 1.031)
EuroSCORE II *	-	1.054 (1.022 – 1.088)	1.053 (1.020 – 1.087)
CBP duration	-	1.004 (0.999 – 1.010)	1.005 (0.999 – 1.011)
Aorta clamping duration	-	1.000 (0.993 – 1.007)	0.999 (0.992 – 1.007)
Hemoglobin concentrations			
Preoperative	-	0.869 (0.793 – 0.952)	0.867 (0.789 – 0.953)

Postoperative	-	0.888 (0.772 – 1.022)	0.892 (0.774 – 1.028)
BMI	-	1.000 (0.996 – 1.003)	1.000 (0.996 – 1.003)
Stay			
ICU	-	1.071 (1.030 – 1.114)	1.089 (1.041 – 1.140)
Hospital	-	0.999 (0.986 – 1.012)	0.997 (0.983 – 1.012)
Death	-	1.934 (0.639 – 5.849)	1.478 (0.432 – 5.060)
Gender	-	-	1.381 (0.935 – 2.040)
Maximum SR	-	-	1.000 (0.992 – 1.007)

AKI = acute kidney injury; $rScO_2$ = regional cerebral oxygen saturation; CBP = cardiopulmonary bypass; BMI = body mass index; ICU = intensive care unit; SR = suppression ratio; CI = confidence interval.

* EuroSCORE II predicts the risk of mortality for patients undergoing cardiac surgery. It is calculated based on 18 different criteria, each associated with an added percentage risk. The score is a percentage. A higher score indicates a higher risk of mortality when undergoing cardiac surgery.

† The patients' $rScO_2$ was measured from electrodes on the left and right frontal lobes. The average between the two was calculated and used for statistical analysis.

Discussion

Methodology

Biases

This was a retrospective cohort study. Compared to prospective studies, it requires less time and financing and can allow the study of multiple associations rather than just one. A retrospective study, however, has some disadvantages; no causal relationship can be established, only incidence and odds ratios. All tests made during this study cannot be used to prove a relationship, but they can help indicate a potential association between two events, in this case the occurrence of CSR-AKI and the end-of-surgery measurements from a cerebral NIRS.

Because no more measurements could be taken, the data was assumed to be correct and complete. Some errors, though, were corrected during the organization and analysis of the dataset due to misplaced commas. These were only corrected based on the normal values for the given variable and associated measures for that patient if possible. For example, normal serum creatinine concentrations vary between approximately 0.6 to 1.2mg/dL for men and between 0.5 to 1.1 mg/dL for women (Hosten 1990). In our dataset, a patient showed a preoperative serum creatinine level of an unrealistic 6.3 mg/dL but completely normal values in the postoperative period. Therefore, the value was changed to 0.63 mg/dL. Less than 10 patients had one value altered by the decimal position. Some patients had missing data for some variables and were excluded from the study.

Lastly, because CSR-AKI has multiple causes, many factors can influence the relationship between the NIRS' measures and its predicting abilities for CSR-AKI. In order to take these interactions into account, a multivariate model was constructed using the variables from this study. However, additional factors may influence the development of CSR-AKI, such as preexisting cardiac disorders or previous cardiac surgeries, the type of cardiac surgery being undergone, diabetes, or the intake of medication (Olivero et al. 2012). These were not included in this study but could be important influencers of the association between the NIRS' measures and its predicting abilities for CSR-AKI and should be studied further.

CSR-AKI incidence

The incidence of CSR-AKI in patients was found to reach 35 to 45% in adults (Bhat et al. 1976; Choi et al. 2014; Graziani et al. 2019). In our study, 210 out of 2,020 patients were labeled as having CSR-AKI based on the AKIN model, meaning a 10.4% incidence between 2006 and 2019 in the cardiac surgery department at the Cliniques Universitaires Saint-Luc. This lower incidence can be explained by many factors, such as a low incidence rate in the sample of our study, loss of precision due to missing data on patients after their stay, or a misclassification of the patient's AKI stage.

To correct these possible errors, a couple of modifications can be made. Firstly, the patient data came from retrospective studies using only patients in the cardiac surgery department. Patients undergoing urgent cardiac surgery were not considered in this study. These patients may be at higher risk and therefore may increase the incidence of CSR-AKI when taken into the study. These patients could be included in order to have a broader significance, as the sample will be enlarged and may help support, strengthen, or oppose the results of this study.

Secondly, to verify each patient's AKI stage based on their clinical measurements, a study using another method, such as the risk-injury-failure-loss-end stage (RIFLE) model could be investigated. While it is very similar to the AKIN model, it also includes criteria based on the GFR (Lu et al. 2022), which could shift non-AKI patients into a positive AKI stage. If there is a significant change, the specificity and sensibility of both models should be calculated to determine which model best classifies patients and continue the study with the best model.

Lastly, the patients being analyzed in this study did not have follow-up data other than serum creatinine levels throughout the week following cardiac surgery. The only basis for classifying patients into groups is based on the serum creatinine concentration measured and the AKIN model. There is no proof that the patients who were labeled as having AKI in this study developed it after their cardiac surgery. A continuation of this study could include a follow-up of these patients to determine if any renal complications occurred after their cardiac surgery and create new groups based on a medical diagnosis.

CSR-AKI incidence in severely desaturated patients

In patients who developed a cerebral desaturation of 20% or more, 9 patients out of 55 were labeled as CSR-AKI, thus an incidence of 16.4%. The rate was increased from 10.4% to

16.4%, which was expected as increased cerebral desaturation can lead to more complications, including CSR-AKI (Fischer et al. 2011). However, since patients in the total sample were expected to have a 35 to 45% incidence rate, an even higher rate was expected for the severely desaturated patients.

A lower incidence could have been caused by the same factors as the ones mentioned above. Additionally, it is important to note that studies analyzing severe cerebral desaturation do not always have the same definition, so there is not a clear expected incidence rate for this measure. Our study defined "severe cerebral desaturation" as a drop of $rScO_2$ of 20% or more from the patient's preoperative value (or baseline value), but some studies defined it as a value of $rScO_2$ that is less than 70% of the baseline $rScO_2$ for more than 150 minutes (Murkin et al. 2007) whereas newer studies used an $rScO_2$ of 50% or less for 30 minutes on either side (Francoeur et al. 2022).

Due to this, our incidence rate may be correct for this sample, but it cannot be directly compared to other studies using other definitions of severe cerebral desaturation.

Urine output

The AKIN model uses variations of serum creatinine concentrations that are all calculated from a baseline value measured before surgery. These factors are used as they reflect the kidneys' overall health and function. An increase in serum creatinine concentration and a decrease in urine output are symptoms of a deteriorating kidney (Olivero et al. 2012). The AKIN model labels patients in three stages depending on the severity of the measurements, with stage 3 being the most severe (Cruz, Ricci, and Ronco 2009).

In our study, no records were found regarding the patients' urine output, so the classification was made using only the creatinine criteria. Using this variable alone can already give a good basis for a diagnostic, but with the addition of urine output, sensitivity increases (Silva et al. 2021). Furthermore, the urine output criteria could help predict a higher risk of mortality, regardless of the serum creatinine concentrations (Petäjä et al. 2017), making it an important factor to consider.

Without using the urine output, there is a potential for underdiagnosis and mislabeling of patients in our study. This missing data can reduce the number of patients labeled as having AKI and alter the statistical tests and analysis. Unfortunately, since no records were found for the patients in our study, this adjustment will have to be done with another sample.

Results

Preoperative measurements

A first analysis was made on variables tested before surgery. Among those, the majority were found to be different between patients who developed CSR-AKI and those who did not.

An increased mean $rScO_2$ before surgery was associated with lower odds of developing CSR-AKI. This measure was also significantly different in patients undergoing severe cerebral desaturation, with a median lower in patients with AKI. These results are in alignment with studies showing that high $rScO_2$ measured before cardiac surgery is associated with the development of complications (Heringlake et al. 2011).

Decreased hemoglobin concentrations were also associated with higher odds of CSR-AKI. Preoperative anemia can triple the risk of postoperative renal dysfunction (Miceli et al. 2014); therefore, it is not surprising to see that preoperative hemoglobin concentrations are inversely linked with CSR-AKI.

Age, preoperative serum creatinine concentration, and EuroSCORE II were, when increased, all associated with increased odds of CSR-AKI. When EuroSCORE II is high, the patient is at a greater risk of mortality, and it has been found to be able to predict postoperative complications, including renal failure (Toumpoulis et al. 2005). Another model using various clinical measurements was created to estimate a patient's GFR, which is currently the best index for overall renal health and function. This model associates older age with a lowered GFR (Levey et al. 1999) and therefore a lowered renal function, in accordance with our study. The preoperative serum creatinine concentrations were higher in patients with CSR-AKI, possibly hinting at an increased risk even when the levels remain in a normal range, similarly to the results from Mao et al. (2013). However, in patients undergoing a severe cerebral desaturation, preoperative creatinine concentration were not changed between AKI and non-AKI patients. Interestingly, the median in AKI patients was lower than patients with no AKI. This may suggests that creatinine elevation is linked to severe cerebral desaturations, but this study isn't adapted to this research and would have to be studied.

From these results, we can recommend that age, preoperative serum creatinine, mean $rScO_2$, EuroSCORE II, and preoperative hemoglobin levels be measured before surgery to help establish a patient's risk, better prepare them during surgery, and keep a closer eye on higher-risk patients and their health thereafter.

Sex and BMI were not found to have an effect on the development of CSR-AKI. In a study by Billings et al. (2012), BMI has been found to be a risk factor for patients undergoing cardiac surgery, with an increased odds of developing CSR-AKI of 1.265 when a patient's BMI increases by 5-kg/m^2. Our study investigated changes in BMI of 1-kg/m^2, which may be too small of an interval to find a significant effect on the development of CSR-AKI. Additionally, the sample in the study mentioned above had patients with a BMI closer to obesity than our sample. Gender also did not seem to alter the development of CSR-AKI in our study, although many other studies have shown its effect (Olivero et al. 2012; Thakar et al. 2003). The sample in our study contained a majority of men overall (71.6%) and in the AKI and non-AKI groups (72.9%; 71.4%). The smaller percentage of women in this study may have caused this lack of significance, and a sample with more equality between the genders may resolve this issue.

From our results, sex and BMI are not factors to take into account when preparing a patient for cardiac surgery, but since studies have found them to be associated with CSR-AKI it would be judicious to keep using them to estimate risk. These variables are, in any case, already written in a patient's file and do not require more tests; therefore, they are ready for use and may help establish a more integrated risk assessment.

Postoperative measurements

An increased mean $rScO_2$ measured at the end of surgery was associated with decreased odds of developing CSR-AKI (odds ratio: 0.968; 95% CI: 0.948 to 0.977). In patients undergoing severe cerebral desaturations, the $rScO_2$ measured on each side and as a mean were all different between AKI and non-AKI patients. In accordance with our hypothesis, as $rScO_2$ increases in a patient, they have a lower risk of developing CSR-AKI. Therefore, analyzing this value towards the end of surgery may help assess the patient's probability of CSR-AKI and highlight higher-risk patients quickly after their surgery, allowing better preparation from the medical team to avoid potentially severe renal complications.

All other variables also showed to be associated with the development of CSR-AKI except for the maximum AUC and maximum SR. While these two measurements are still essential to cardiac surgery and will continue to be used to monitor cerebral health, they do not appear to help predict CSR-AKI. The variables maximum serum creatinine concentration,

stay in ICU, hospital, mortality, postoperative hemoglobin concentration, CPB, and AoC were all associated with CSR-AKI.

Hemoglobin concentrations have a natural tendency to fall after cardiac surgery (George et al. 2012), which can be seen in our study as well. Nevertheless, the levels in patients who developed CSR-AKI were significantly lower than those in non-AKI patients, and this slight decrease may hint at its development.

An important risk factor during cardiac surgery is its duration, and in particular the duration of the CPB and the AoC. A 30-minute increase in CPB can increase the chance of developing renal complications (Salis et al. 2008). Furthermore, regardless of the patient's risk, a longer AoC increased the likelihood of renal complications (Al-Sarraf et al. 2011). Our study showed similar results, with increased odds of developing CSR-AKI for each minute of CPB and AoC added.

A patient's development of CSR-AKI was associated with an increased stay in the ICU and hospital and higher mortality. Hospital and ICU stays have been found to be increasing and associated with changes in SO_2. Fischer et al. (2011) found a 3-day increase in the ICU and a 4-day increase in the hospital when patients had lowered SO_2 levels. Chertow et al. (2005) have also found an increasing length of stay and mortality in patients who developed CSR-AKI at increasing serum creatinine concentrations. Mortality rates were more than 9 times higher in patients with CSR-AKI. These results are expected and well known (Thakar et al. 2003; Graziani et al. 2019; Bellomo, Kellum, and Ronco 2012; Fischer et al. 2011; Chertow et al. 2005). Our results confirm these observations and emphasize the need for a prediction tool for CSR-AKI, as longer stay will increase the patient's mortality risk and cost greatly to both the patient and the hospital (Chertow et al. 2005).

Lastly, many studies have defined a large increase in serum creatinine concentration during surgery as a symptom of AKI (Lassnigg et al. 2004; Praught and Shlipak 2005). Our results here show the maximal postoperative serum creatinine concentration was associated with CSR-AKI, even when patients underwent a severe cerebral desaturation, indicating that looking at their levels at the end of surgery may help indicate the development of this, as higher concentrations are associated with CSR-AKI. This difference seems to conform to the current diagnosis methods for CSR-AKI, which includes a follow-up measurement of creatinine levels following surgery to identify any increasing change.

Adjusted model for mean postoperative $rScO_2$

Two logistic models in this study showed a significant mean postoperative $rScO_2$ in association with CSR-AKI. By looking at each model's likelihood, Model 1 is the best fit for our data. However, by looking at the Akaike Information Criterion and Bayesian Information Criterion, Model 3 is a better fit. Therefore, Model 3 should be considered the most suitable model of the three to investigate mean postoperative $rScO_2$.

In this multivariate model, the mean postoperative $rScO_2$ was found to have a significant association with CSR-AKI. This model shows that this measurement could help physicians predict renal injuries following cardiac surgery even when taking other factors into account such as age, EuroSCORE II, preoperative hemoglobin concentration, and ICU stay. These variables, as mentioned above, were expected to be correlated to CSR-AKI, as it has already been identified in other studies. Other parameters, such as CBP duration, AoC duration, postoperative hemoglobin levels, BMI, hospital stay, and mortality, were not shown to be associated with CSR-AKI either.

Postoperative hemoglobin levels were not found to be associated with CSR-AKI. As mentioned above, their levels tend to fall after surgery, which was seen in our study as well, but they do not seem to be a risk factor. In fact, 79% of patients who experience this drop recover before their discharge (George et al. 2012). Therefore, this measurement should not be used to assess renal injury following cardiac surgery, as a drop in hemoglobin levels after surgery is not specific to CSR-AKI.

In our study, the parameters CPB duration, AoC duration, BMI, hospital stay, mortality, gender, and maximum SR also demonstrated no association with CSR-AKI, which has some conflicting results in comparison to other studies (Salis et al. 2008; Olivero et al. 2012; Al-Sarraf et al. 2011; Graziani et al. 2019; Bhat et al. 1976). Since this study's main objective was to investigate the use of the NIRS measurement taken at the end of surgery to assess a patient's risk of CSR-AKI, these variables may not have been properly studied.

CPB duration and AoC duration were both studied as continuous variables, but it may be interesting to look at them by time intervals instead. For example, Salis et al. (2008) looked at outcomes associated with a 30-minute increase in CPB duration. Using a 1-minute change to estimate association with CSR-AKI may be too slim of a measure, in particular when the average time of CPB and AoC is 105 and 77 minutes, respectively. The statistical tests will not describe the larger trends that may exist and limit a comprehensive analysis of these variables during cardiac surgery. Similarly, and as mentioned above, a patient's BMI

may have been unsignificant in this study for the same reasons and may need to be recalculated by intervals rather than by a 1-kg/m^2 change.

An increased BMI has been associated with an increased risk of CSR-AKI, in particular when patients have a BMI higher than 24.0, or obese (Shi et al. 2020). Our model does not show an association between BMI and CSR-AKI, but this can be justified by two points. First, studies looking at BMI tend to look at it as a categorical variable by separating patients' BMI by intervals. In our study, this was not done, and we analyzed BMI as a continuous variable. Second, the sample of our study had a large mean BMI, with the majority of patients having one higher than 24.0. Therefore, our sample may not be ideal to investigate this variable as our sample's BMIs are not diverse enough.

Hospital stay, in our study, was not associated with CSR-AKI, unlike ICU stay. A possible explanation for this may be that the CUSL allows patients to have a longer stay to recover from their surgery, regardless of renal complications or the severity of renal complications. If severe CSR-AKI does appear in a patient, they will be quickly transferred to the ICU to be properly treated, and luckily, they are able to recover. This hypothesis may also be explained the proportions in each stage of CSR-AKI. Around 7.3% of patients developed stage 1 CSR-AKI, 1.6% stage 2, and 1.5% stage 3. Patients in higher stages will require more long-term treatments, such as dialysis, while patients in lower stages may simply need acute medication. This study did not differentiate between the three stages; therefore, patients needing shorter or fewer consultations may have influenced the length of hospital stay in relation to the presence of CSR-AKI.

CSR-AKI is associated with higher mortality rates, and our study noted a patient's death during their stay around their surgery. This window is quite small and may not represent the injury's fatality through time accurately. Additionally, the mortality rate caused by cardiac surgery alone is a factor to consider, which was not in this study, and it may have altered the patients' cause of death. According to Thongprayoon et al. (2020), different types of cardiac surgery have different mortality rates associated with them. This was not investigated in this study and may have led to the insignificance of our mortality rates.

Gender was already found to not be associated with CSR-AKI in our study. A sample containing a more balanced number of both genders may show a difference between the two and be in accordance with other studies stating that women are more at risk. Our study does not show these results.

Lastly, the maximum SR measured did not have an association with CSR-AKI. This may indicate that a patient's periods of low brain voltage are not associated with any renal

complications during surgery. They do not seem to be useful either alone or in a model to determine a patient's possible onset of CSR-AKI.

Conclusion

Measurements of a patient's $rScO_2$ taken at the end of surgery are associated with the development of AKI following cardiac surgery. This relationship stays true when other variables are taken into account, such as age, gender, BMI, EuroSCORE II, pre- and postoperative hemoglobin concentration, ICU stay, hospital stay, CBP duration, AoC duration, maximum SR, and mortality. While an increase in $rScO_2$ of 1% would only change a patient's odds by 0.982, larger changes will have a more prominent effect on the patient's future.

Our study highlights the usefulness of using NIRS measurements to possibly detect renal complications in addition to monitoring brain saturation. It may help physicians in the surgery room better estimate the patient's odds and be able to anticipate possible action following surgery. This way, a patient may develop a lower-stage CSR-AKI or other shorter-term renal injuries if they are identified and treated quickly. Additionally, the use of an NIRS during surgery is non-invasive and simple to use. The patient will not be placed at a greater risk, and physicians can track the patient's rScO2 effortlessly. This is greatly beneficial to both sides, as other methods, such as measuring biomarkers, are invasive and require more time and expertise to be properly executed.

Our study only shows an association between the two, but there is potential for studying the exact relationship between brain oxygen balance and renal complications following cardiac surgery. With such high incidence rates and high risk for the patient, monitoring their health and their kidneys is crucial, and finding an early detection system sounds promising. The NIRS may help to do so, but further studies have to confirm these results.

Perspective

This study showed potential for the use of NIRS during cardiac surgery, but more studies need to be completed to confirm and identify its exact use with regards to CSR-AKI.

Firstly, while our results are significant, the lack of urine measurement is crucial in the diagnosis of CSR-AKI. Without this, we may have underdiagnosed patients in our sample, and our results may alter due to this. Therefore, new studies should include this measurement to properly identify each patient's condition.

Secondly, a study using a broader sample may help overcome some biases. Some variables were not found to be linked to CSR-AKI, although they have been proven to be risk factors in many other studies. This difference is most likely due to a sampling bias, for example, in regards to gender. It would be interesting to look at patients from a larger sample, even from various hospitals, or by including urgent cardiac surgeries, to have a group that will more closely resemble the real population.

Thirdly, some variables were not analyzed properly, and changing continuous variables to intervals may display risk factors in a new way. In our study, BMI was not associated with CSR-AKI, but high BMIs have been found to be a risk factor. Since we did not consider the different categories of BMI, we did not find the same result. By doing this, we expect the variable as such to be significant, but it may also highlight some variables' increased risk as they become more extreme.

Lastly, CSR-AKI can evolve very differently from one patient to another, as can their morbidities as well. Our study did not look at separating patients who developed severe CSR-AKI from those who developed mild CSR-AKI. It could be interesting to separate the AKI group into each stage to differentiate factors that cause a severe risk or only a mild risk for the patient. If significant differences are found between these three categories, a study looking even further could use the RIFLE model instead of AKIN to have a better look at the possible evolution of CSR-AKI.

Overall, this study showed an interesting look at the NIRS as a means of detecting CSR-AKI in addition to measuring brain oxygen balance during cardiac surgery. While the study does have some limitations, the subject deserves some insights and a further look into its potential.

Abbreviations

AKI	Acute Kidney Injury
AKIN	Acute Kidney Injury Network
AoC	Aorta Clamping
ARF	Acute Renal Failure
AUC	Area Under the Curve
BMI	Body Mass Index
CPB	Cardiopulmonary Bypass
CUSL	Cliniques Universitaires Saint-Luc
CSR-AKI	Cardiac Surgery-Related Acute Kidney Injury
EuroSCORE II	European System for Cardiac Operative Risk Evaluation II
GFR	Glomerular Filtration Rate
Hb	Hemoglobin
ICU	Intensive Care Unit
IRA	Insuffisance Rénale Aiguë
IRA-PO	Insuffisance Rénale Aiguë Post-Opératoire
NIRS	Near-Infrared Spectroscopy
OR	Odds Ratio
RAAS	Renin-Angiotensin-Aldosterone System
RRT	Renal Replacement Therapy
rSO_2	Regional Oxygen Saturation
rScO2	Regional Cerebral Oxygen Saturation
SO_2	Oxygen Saturation
SPIR	Spectroscopie proche infrarouge
StO_2	Tissue Oxygen Saturation
SR CH1/2	Suppression Ratio Channel 1 or 2

Bibliography

Al-Sarraf, Nael, Lukman Thalib, Anne Hughes, Maighread Houlihan, Michael Tolan, Vincent Young, and Eillish McGovern. 2011. 'Cross-clamp time is an independent predictor of mortality and morbidity in low- and high-risk cardiac patients', *International Journal of Surgery*, 9: 104-09.

Balci, C., E. Haftaci, and A. T. Kunt. 2018. 'Use of cerebral oxygen saturation and hemoglobin concentration to predict acute kidney injury after cardiac surgery', *J Int Med Res*, 46: 1130-37.

Bellomo, R., J. A. Kellum, and C. Ronco. 2012. 'Acute kidney injury', *Lancet*, 380: 756-66.

Bhat, J. Ganesh, Melvin C. Gluck, Jerome Lowenstein, and David S. Baldwin. 1976. 'Renal Failure After Open Heart Surgery', *Annals of Internal Medicine*, 84: 677-82.

Billings, Frederic T. th, Mias Pretorius, Jonathan S. Schildcrout, Nathaniel D. Mercaldo, John G. Byrne, T. Alp Ikizler, and Nancy J. Brown. 2012. 'Obesity and oxidative stress predict AKI after cardiac surgery', *Journal of the American Society of Nephrology : JASN*, 23: 1221-28.

Chertow, G. M., E. Burdick, M. Honour, J. V. Bonventre, and D. W. Bates. 2005. 'Acute kidney injury, mortality, length of stay, and costs in hospitalized patients', *J Am Soc Nephrol*, 16: 3365-70.

Cheung, A., L. Tu, A. Macnab, B. K. Kwon, and B. Shadgan. 2022. 'Detection of hypoxia by near-infrared spectroscopy and pulse oximetry: a comparative study', *J Biomed Opt*, 27.

Choi, Dae-Kee, Wook-Jong Kim, Ji-Hyun Chin, Eun-Ho Lee, Kyung Don Hahm, Ji Yeon Sim, and In Cheol Choi. 2014. 'Intraoperative Renal Regional Oxygen Desaturation Can Be a Predictor for Acute Kidney Injury after Cardiac Surgery', *Journal of Cardiothoracic and Vascular Anesthesia*, 28: 564-71.

Cruz, D. N., Z. Ricci, and C. Ronco. 2009. 'Clinical review: RIFLE and AKIN--time for reappraisal', *Crit Care*, 13: 211.

Edmonds, Harvey L. 2018. "DETECTION AND CORRECTION OF BRAIN OXYGEN IMBALANCE." In.

Fischer, G. W., H. M. Lin, M. Krol, M. F. Galati, G. Di Luozzo, R. B. Griepp, and D. L. Reich. 2011. 'Noninvasive cerebral oxygenation may predict outcome in patients undergoing aortic arch surgery', *J Thorac Cardiovasc Surg*, 141: 815-21.

Francoeur, Charles L., François Lauzier, Patrice Brassard, and Alexis F. Turgeon. 2022. 'Near Infrared Spectroscopy for Poor Grade Aneurysmal Subarachnoid Hemorrhage—A Concise Review', *Frontiers in Neurology*, 13.

George, T. J., C. A. Beaty, A. Kilic, K. A. Haggerty, S. M. Frank, W. J. Savage, and G. J. Whitman. 2012. 'Hemoglobin drift after cardiac surgery', *Ann Thorac Surg*, 94: 703-9.

Grams, Morgan E., and Hamid Rabb. 2012. 'The distant organ effects of acute kidney injury', *Kidney International*, 81: 942-48.

Graziani, M. P., M. Moser, C. M. Bozzola, H. M. Gálvez, J. Irman Garrido, P. G. Álvarez, and M. L. Fernie. 2019. 'Acute kidney injury in children after cardiac surgery: Risk factors and outcomes. A retrospective, cohort study', *Arch Argent Pediatr*, 117: e557-e67.

Hazle, M. A., R. J. Gajarski, R. Aiyagari, S. Yu, A. Abraham, J. Donohue, and N. B. Blatt. 2013. 'Urinary biomarkers and renal near-infrared spectroscopy predict intensive care unit outcomes after cardiac surgery in infants younger than 6 months of age', *J Thorac Cardiovasc Surg*, 146: 861-67.e1.

Heringlake, M., C. Garbers, J. H. Käbler, I. Anderson, H. Heinze, J. Schön, K. U. Berger, L. Dibbelt, H. H. Sievers, and T. Hanke. 2011. 'Preoperative cerebral oxygen saturation and clinical outcomes in cardiac surgery', *Anesthesiology*, 114: 58-69.

Hosten, A. O. 1990. 'BUN and Creatinine.' in H. K. Walker, W. D. Hall and J. W. Hurst (eds.), *Clinical Methods: The History, Physical, and Laboratory Examinations* (Butterworths

Copyright © 1990, Butterworth Publishers, a division of Reed Publishing.: Boston).

Lassnigg, A., D. Schmidlin, M. Mouhieddine, L. M. Bachmann, W. Druml, P. Bauer, and M. Hiesmayr. 2004. 'Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study', *J Am Soc Nephrol*, 15: 1597-605.

Levey, A. S., J. P. Bosch, J. B. Lewis, T. Greene, N. Rogers, and D. Roth. 1999. 'A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group', *Ann Intern Med*, 130: 461-70.

Lu, C., J. Lian, Z. Cao, L. Chen, J. Liang, and S. Wang. 2022. 'Comparing the pRIFLE, AKIN, KDIGO, and modified KDIGO criteria in neonates after cardiac surgery', *Pediatr Nephrol*, 37: 1399-405.

Magasich-Airola, N. P., M. Momeni, C. Sanchez Torres, C. De Magnée, R. Tambucci, R. Reding, and T. Pirotte. 2022. 'Regional oxygen saturation measured by two different oximetry monitors in infants and children undergoing living donor liver transplantation with bilirubin measurements: A prospective observational study', *Paediatr Anaesth*.

Mao, H., N. Katz, W. Ariyanon, L. Blanca-Martos, Z. Adýbelli, A. Giuliani, T. H. Danesi, J. C. Kim, A. Nayak, M. Neri, G. M. Virzi, A. Brocca, E. Scalzotto, L. Salvador, and C. Ronco. 2013. 'Cardiac Surgery-Associated Acute Kidney Injury', *Cardiorenal Medicine*, 3: 178-99.

Martin, Daniel, Denny Levett, Rick Bezemer, Hugh Montgomery, and Michael Grocott. 2013. 'The Use of Skeletal Muscle Near Infrared Spectroscopy and a Vascular Occlusion Test at High Altitude', *High altitude medicine & biology*, 14: 256-62.

Mehta, R. L., J. A. Kellum, S. V. Shah, B. A. Molitoris, C. Ronco, D. G. Warnock, and A. Levin. 2007. 'Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury', *Crit Care*, 11: R31.

Miceli, Antonio, Francesco Romeo, Mattia Glauber, Paolo M. de Siena, Massimo Caputo, and Gianni D. Angelini. 2014. 'Preoperative anemia increases mortality and postoperative morbidity after cardiac surgery', *Journal of Cardiothoracic Surgery*, 9: 9050.

Murkin, J. M., and M. Arango. 2009. 'Near-infrared spectroscopy as an index of brain and tissue oxygenation', *Br J Anaesth*, 103 Suppl 1: i3-13.

Murkin, John M., Sandra J. Adams, Richard J. Novick, Mackenzie Quantz, Daniel Bainbridge, Ivan Iglesias, Andrew Cleland, Betsy Schaefer, Beverly Irwin, and Stephanie Fox. 2007. 'Monitoring Brain Oxygen Saturation During Coronary Bypass Surgery: A Randomized, Prospective Study', *Anesthesia & Analgesia*, 104: 51-58.

Olivero, J. J., J. J. Olivero, P. T. Nguyen, and A. Kagan. 2012. 'Acute kidney injury after cardiovascular surgery: an overview', *Methodist Debakey Cardiovasc J*, 8: 31-6.

Owens, G. E., K. King, J. G. Gurney, and J. R. Charpie. 2011. 'Low renal oximetry correlates with acute kidney injury after infant cardiac surgery', *Pediatr Cardiol*, 32: 183-8.

Patel, Seema, Abdur Rauf, Haroon Khan, and Tareq Abu-Izneid. 2017. 'Renin-angiotensin-aldosterone (RAAS): The ubiquitous system for homeostasis and pathologies', *Biomedicine & Pharmacotherapy*, 94: 317-25.

Petäjä, L., S. Vaara, S. Liuhanen, R. Suojaranta-Ylinen, L. Mildh, S. Nisula, A. M. Korhonen, K. M. Kaukonen, M. Salmenperä, and V. Pettilä. 2017. 'Acute Kidney

Injury After Cardiac Surgery by Complete KDIGO Criteria Predicts Increased Mortality', *J Cardiothorac Vasc Anesth*, 31: 827-36.

Polderman, Kees. 2019. 'Cerebral Monitoring May Aid Assessment of Brain Function During Cardiac Arrest', *Journal of Emergency Medical Services*.

Praught, M. L., and M. G. Shlipak. 2005. 'Are small changes in serum creatinine an important risk factor?', *Curr Opin Nephrol Hypertens*, 14: 265-70.

Ronco, C., R. Bellomo, and J. Kellum. 2017. 'Understanding renal functional reserve', *Intensive Care Med*, 43: 917-20.

Salis, S., V. V. Mazzanti, G. Merli, L. Salvi, C. C. Tedesco, F. Veglia, and E. Sisillo. 2008. 'Cardiopulmonary bypass duration is an independent predictor of morbidity and mortality after cardiac surgery', *J Cardiothorac Vasc Anesth*, 22: 814-22.

Shi, N., K. Liu, Y. Fan, L. Yang, S. Zhang, X. Li, H. Wu, M. Li, H. Mao, X. Xu, S. P. Ma, P. Xiao, and S. Jiang. 2020. 'The Association Between Obesity and Risk of Acute Kidney Injury After Cardiac Surgery', *Front Endocrinol (Lausanne)*, 11: 534294.

Silva, T. F. D., Krdc Silva, C. M. Nepomuceno, C. S. M. Corrêa, J. P. M. Godoy, Atld Santos, and A. S. Gheller. 2021. 'Incidence of acute kidney injury post cardiac surgery: a comparison of the AKIN and KDIGO criteria', *Braz J Anesthesiol*, 71: 511-16.

Thakar, C. V., O. Liangos, J. P. Yared, D. Nelson, M. R. Piedmonte, S. Hariachar, and E. P. Paganini. 2003. 'ARF after open-heart surgery: Influence of gender and race', *Am J Kidney Dis*, 41: 742-51.

Thongprayoon, C., P. Hansrivijit, K. Kovvuru, S. R. Kanduri, A. Torres-Ortiz, P. Acharya, M. L. Gonzalez-Suarez, W. Kaewput, T. Bathini, and W. Cheungpasitporn. 2020. 'Diagnostics, Risk Factors, Treatment and Outcomes of Acute Kidney Injury in a New Paradigm', *J Clin Med*, 9.

Toumpoulis, Ioannis K., Constantine E. Anagnostopoulos, Daniel G. Swistel, and Joseph J. DeRose, Jr. 2005. 'Does EuroSCORE predict length of stay and specific postoperative complications after cardiac surgery?', *European Journal of Cardio-Thoracic Surgery*, 27: 128-33.

Wallace, M. A. 1998. 'Anatomy and physiology of the kidney', *Aorn j*, 68: 800, 03-16, 19-20; quiz 21-4.

Wang, Y., and R. Bellomo. 2017. 'Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment', *Nat Rev Nephrol*, 13: 697-711.

Acute kidney injury (AKI) is linked to multiple morbidities and an increased mortality rate. It is a common cardiac surgery-related complication. Early diagnosis could limit the progression of AKI, but current screening techniques are still limiting. However, new studies are focusing on the application of near-infrared spectroscopy (NIRS). The device is connected to electrodes that are placed on the skin to measure the regional oxygen saturation (rSO_2). This study investigates an association between NIRS measurements of the brain's regional oxygen saturation at the end of cardiac surgery and the onset of cardiac surgery-related acute kidney injury (CSR-AKI).

The data for this retrospective study was taken from 2020 patients undergoing cardiac surgery at the Cliniques Universitaires Saint-Luc between 2006 and 2019. Following the criteria of the Acute Kidney Injury Network (AKIN) classification, 10.6% (210) of the patients were classified as having developed CSR-AKI. Multiple variables were compared, including mean preoperative and postoperative cerebral rSO_2, the most determining variable in this study. In addition, a second study was carried out among patients who presented cerebral desaturation during the operation of at least 20%. Lastly, a multivariate analysis was performed to look at the effect of the measurements taken by NIRS in a more comprehensive model.

The cerebral rSO_2 ($rScO_2$) of 2020 patients was measured throughout cardiac surgery using an INVOS^{TM} cerebral NIRS. The average postoperative cerebral rSO_2 was associated with a lower measure in patients who developed CSR-AKI than in patients who did not. The other variables also showed a significant odds ratio except for sex, body mass index (BMI), maximum area under the curve (AUC) and maximum suppression ratio (SR). Comparable results were observed in the group of patients with cerebral desaturation during the operation of at least 20%. In the multivariate analysis, the postoperative $rScO_2$ taken by NIRS was significant.

Measurements of $rScO_2$ by the NIRS at the end of cardiac surgery have the potential to help physicians predict the onset of CSR-AKI. However, its exact relationship between regional cerebral oxygen saturation and the occurrence of AKI requires further studies.