PCO2 gap is a good marker to predict cardiac surgery associated-acute kidney injury (CSA-AKI)

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Abstract

***Objective*: To identify the correlation between arterial-venous carbon dioxide partial pressure difference (PCO2 gap) and cardiac surgery associated-acute kidney injury (CSA-AKI) in Dr. Wahidin Sudirohusodo Hospital.**

***Design*: This was an observational analytical study with a prospective approach and cohort study design.**

***Setting*: The study was conducted in the Cardiac Centre of Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia, from December 2024 to February 2025.**

***Patients*: The population of this study was all patients who underwent open heart surgery at Dr. Wahidin Sudirohusodo Hospital.**

***Measurements*: We measured the PCO2 gap from blood gas analysis and urinary neutrophil gelatinase-associated lipocalin (NGAL) before incision and following the surgical procedure (2 hours following off of the cardiopulmonary bypass [CPB] or graft implanted for off bypass procedure). We also observed urine output and serum creatinine in the first 48 hours following surgery to diagnose acute kidney injury (AKI) according to the Kidney Disease Improving Global Outcomes (KDIGO) classification.**

***Results*: There was a significant difference in PCO2 gap following surgical procedure between the AKI and non-AKI groups (p=0.004), with the PCO2 gap found to be higher in the AKI group at 7.76±2.22 vs 4.61±2.21. PCO2 gap was also found to be highly correlated to AKI incidence (ρ=0.604, p<0.003).**

The receiver operating characteristic (ROC) curve found that the PCO2 gap following surgical procedure cut-off point value to determine the incidence of AKI was 5.7 mmHg (sensitivity 87.5%, specificity 78.6%) with 81.8% accuracy (OR=25.6). The ROC curve also found that NGAL following surgical procedure cut-off point value to determine the incidence of AKI was 100.09 ng/ml (sensitivity 87.5%, specificity 85.7%) with 86.4% accuracy.

***Conclusions*: A higher PCO2 gap following a surgical procedure correlated to AKI following open heart surgery. The PCO2 gap following a surgical procedure was a good marker to predict AKI incidence, with a cut-off point value as high as 5.7 mmHg, which was not better than NGAL.**

Keywords: PCO2 gap, NGAL, AKI, cardiac surgery, CSA-AKI.

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Background

Acute kidney injury (AKI) is a global health issue, with an estimated incidence of 13.3 million cases per year. (1) AKI is one of the complications that can occur following cardiac surgery, with a reported incidence of up to 50%. (2) It contributes to approximately 1.7 million deaths annually and significantly increases the risk of progressing to end-stage renal disease. The early mortality rate in AKI patients is around 5%. (1,2) Furthermore, AKI is associated with an increased mortality following open-heart surgery. The mortality rate after cardiac surgery without AKI ranges from 1% to 8%, but it increases more than fourfold in patients who develop AKI. The need for renal replacement therapy further raises the AKI-related mortality rate to 63%. (3)

Cardiac surgery-associated AKI (CAS-AKI) occurs due to a rapid decline in kidney function after surgery, characterized by a significant reduction in glomerular filtration rate. (3) Several factors associated with cardiopulmonary bypass (CPB) contribute to AKI, including CPB duration, low perfusion pressure, low pump flow, severe hemodilution, and low oxygen delivery. Additionally, certain non-modifiable factors increase the risk of AKI, such as advanced age, preoperative renal dysfunction, diabetes, hypertension, peripheral artery disease, chronic lung disease, complex surgeries, and other patient-related factors. (2)

The mechanisms underlying AKI in cardiac surgery mainly involve hypoperfusion, renal ischemia, hemodynamic instability, inflammation, oxidative stress, and hemolysis. (4,5) During major surgery, an increased oxygen demand results from surgical trauma and the body's metabolic response to injury. High-risk patients, particularly those with preexisting cardiac conditions, may be unable to increase cardiac output and oxygen delivery sufficiently. Consequently, these patients are more susceptible to tissue hypoperfusion, severe systemic inflammatory responses, and organ dysfunction-related mortality. (6)

AKI can progress to chronic kidney disease, and even a temporary postoperative increase in serum creatinine is associated with reduced patient survival. Since no effective treatment is currently available for AKI after cardiac surgery, efforts to reduce its incidence have become increasingly crucial to improve patient outcomes. (7) One potential preventive approach involves perioperative risk assessment using early postoperative biomarkers.

The carbon dioxide partial pressure (PCO2) gap refers to the difference between partial pressures of carbon dioxide in arterial and venous blood. It is proportional to carbon dioxide (CO2) production in tissues and inversely related to cardiac output. The normal PCO2 gap ranges from 2 to 6 mmHg. (8) A widened PCO2 gap has been suggested as an indicator of hypoperfusion following open-heart surgery. (9) A study by Silva et al. found that AKI occurred in 27.3% of patients with a PCO2 gap exceeding 5.0 mmHg, whereas the incidence was only 4.5% in patients with a PCO2 gap below 5.0 mmHg. (6) However, research on the association between PCO2 gap and postoperative AKI remains limited, particularly in open-heart surgery. If an increased PCO2 gap is indeed linked to AKI, it could serve as a valuable early biomarker for predicting postoperative AKI and guiding preventive strategies. Therefore, this study aimed to assess the relationship between the PCO2 gap and the incidence of AKI following open-heart surgery at the Cardiac Centre of Dr. Wahidin Sudirohusodo Hospital, Makassar.

Methods

Study design, population, and sampling method

This study was an analytical observational study with a prospective cohort design. It was conducted at the Cardiac Centre of Dr. Wahidin Sudirohusodo Hospital, Makassar, from December 2024 to February 2025.

The study population consisted of all patients undergoing open-heart surgery at Dr. Wahidin Sudirohusodo Hospital. The study sample included patients scheduled for open-heart surgery at the same hospital who met the inclusion criteria and agreed to participate in the study. Sampling was conducted using a consecutive sampling method. The sample size was determined using Harry King's nomogram technique, yielding a minimum required sample size of 22 participants. The inclusion criteria for this study were patients scheduled for open-heart surgery, aged between 18 and 65 years, with a body mass index (BMI) of less than 30 kg/m², and who have signed the informed consent form. The exclusion criteria included patients with diabetes mellitus, preoperative renal dysfunction, peripheral artery disease, chronic lung disease, and those taking nephrotoxic agents such as glycopeptide and aminoglycoside antibiotics or nonsteroidal anti-inflammatory drugs (NSAIDs). Patients with a history of kidney disease or a family history of kidney disease (mother or sister) were also excluded. Patients would be considered dropouts if they died within 48 hours postoperatively or withdrew from the study.

Data collection

Data collection was conducted by enrolling patients who met the inclusion criteria in the order of their arrival until the required sample size was reached.

After all study subjects had signed the informed consent form, intra-arterial blood pressure monitoring was placed in the radial or brachial artery. Subsequently, general anesthesia was administered, followed by the insertion of a central venous catheter into the right subclavian or right internal jugular vein. Arterial blood gas (ABG) samples were collected after the placement of the central venous catheter and intra-arterial pressure monitoring, simultaneously before the surgery began, to assess arterial carbon dioxide partial pressure (PaCO2) and venous carbon dioxide partial pressure (PvCO2), which determine the PCO2 gap. Additionally, a preoperative urine sample was collected after urinary catheter placement to measure preoperative urinary neutrophil gelatinase-associated lipocalin (NGAL) levels. ABG sampling was repeated two hours after grafting was completed in off-pump surgery and two hours after CPB removal in on-pump surgery to reassess PaCO2 and PvCO2. Similarly, urine samples were collected two hours after grafting in off-pump surgery and two hours after CPB removal in on-pump surgery to measure postoperative urinary NGAL levels. Postoperative urine output was monitored for the first 48 hours, and serum creatinine levels were measured 48 hours post-surgery. All data were recorded in the Case Report Form (CRF).

Data analysis

The collected data were processed and presented in narrative form, tables, or graphs, including mean values, standard deviations, frequencies, and percentages, using SPSS 25 for Windows. Data were displayed as frequencies and percentages. Normality testing was conducted using the Shapiro-Wilk test. The correlation between the PCO2 gap, as a continuous variable, and the incidence of AKI were analyzed using the Spearman test. The correlation between the PCO2 gap and AKI as categorical variables was assessed using the Pearson chi-square test. For comparisons between categorical variables, the chi-square test was used if no expected cell count was less than five. If any cell has an expected count below five, Fisher's exact test would be applied. The correlation between the PCO2 gap and urinary NGAL was tested using Pearson's correlation if both variables followed a normal distribution. If one or both variables did not follow a normal distribution, the Spearman test would be used. Diagnostic testing was conducted using the receiver operating characteristic (ROC) curve to determine the area under the curve (AUC), sensitivity, specificity, and cutoff values for the PCO2 gap and urinary NGAL. The tests were performed at a 5% significance level.

Ethical approval

All research procedures were conducted after providing an explanation and obtaining consent from the study participants, who signed an informed consent form. This study has been approved by the Health Research Ethics Committee of the Faculty of Medicine, Hasanuddin University, under approval number 981/UN4.6.4.5.31/PP36/2024.

Results

Sample characteristics

The total sample in this study consisted of 22 patients who underwent open-heart surgery at the Cardiac Centre of Dr. Wahidin Sudirohusodo Hospital, Makassar. Among them, eight patients developed AKI.

Table 1 presents the sample characteristics based on the incidence of AKI after open-heart surgery. There were no significant differences between the AKI and non-AKI groups in terms of age, BMI, metabolic equivalents (METs), New York Heart Association (NYHA) classification, ejection fraction, pulmonary hypertension, central venous pressure (CVP), aortic cross-clamp time (AoX time), and cardiopulmonary bypass (CPB) time. However, low cardiac output, right ventricular systolic dysfunction, and mortality differed significantly between the AKI and non-AKI groups ($p<0.05$).

Table 2 categorizes the sample into two groups based on the preoperative PCO2 gap with a cutoff of 6 mmHg. There were no significant differences between the high and normal PCO2 gap groups regarding age, BMI, METs, NYHA classification, ejection fraction, right ventricular systolic dysfunction, pulmonary hypertension, CVP, AoX time, CPB time, and 7-day mortality. However, low cardiac output and the EuroSCORE differed significantly between the elevated PCO2 gap group and the normal PCO2 gap group ($p<0.05$).

Table 3 categorizes the sample into two groups based on the PCO2 gap measured 2 hours post-CPB removal, with a cutoff of 6 mmHg. Among the analyzed variables, only 7-day mortality showed a significant difference between the high post-CPB PCO2 gap group and the normal group ($p<0.05$). The other variables did not show statistically significant differences between the two groups.

Relationship between PCO2 gap and the incidence of AKI in patients undergoing open-heart surgery

The relationship between the preoperative PCO2 gap and the incidence of AKI indicated that a preoperative PCO2 gap of ≥6 mmHg was not associated with the occurrence of AKI after open-heart surgery. However, a PCO2 gap of ≥6 mmHg meas-

ured 2 hours post-CPB was significantly associated with the incidence of AKI following open-heart surgery, whereas a normal PCO2 gap was associated with the absence of AKI ($p<0.006$) (**Table 4**).

Comparison of PCO2 gap and NGAL in predicting AKI after open-heart surgery

The comparison of the PCO2 gap and NGAL values based on AKI occurrence also included the correlation between AKI and these variables. Significant differences were observed in the change in PCO2 gap 2 hours post-CPB removal, NGAL 2 hours post-CPB removal, NGAL change, and NGAL increase ratio (**Table 5**).

The ROC curves in **Figures 1** and **2** show that the PCO2 gap 2 hours post-CPB and NGAL 2 hours post-CPB yield high AUC of 86.2% and 92%, respectively. Conversely, the AUC values for preoperative PCO2 gap and NGAL remained low (62.1% and 54.5%). As shown in **Table 6**, cutoff values for each parameter are presented along with their sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Table 7 presents the accuracy comparison between the PCO2 gap 2 hours post-CPB and NGAL 2 hours post-CPB in predicting AKI after open-heart surgery. NGAL 2 hours post-CPB was the most accurate variable (86.4% accuracy) in predicting AKI after open-heart surgery.

Discussion

The study sample consisted of 13 men and 9 women, with an age range from 19 to 64 years. A total of 8 subjects (36.4%) developed AKI, and 5 subjects (22.7%) died, all of whom had AKI ($p=0.002$). Among those who experienced AKI, there were 4 men and 4 women. The mean age of subjects with and without AKI was similar, at 43.63±16.76 and 44.29±15.26 years, respectively.

Clinically, there were no statistically significant differences in functional capacity and activity limitations between the AKI and non-AKI groups. This finding aligned with previous studies suggesting that AKI was associated with severe activity limitations (NYHA class IV), primarily due to acute cardiorenal syndrome. Left ventricular function, as reflected by ejection fraction, was also comparable between the two groups. However, a preoperative ejection fraction of less than 40% was identified as a significant risk factor for post-surgical AKI. Severely reduced ejection fraction is a major contributor to AKI through the pathophysiology of cardiorenal syndrome. (10) Additionally, preload parameters, such as CVP, showed no significant differences between the two groups. Right ventricular function, as represented by tricuspid annular plane systolic excursion (TAPSE), was significantly lower in the AKI group, with a median value of 1.8 (1.0-2.0) cm. A decrease in TAPSE reflects impaired right ventricular function, which can lead to venous congestion and an increased incidence of AKI. AKI caused by right ventricular dysfunction has been associated with an almost eightfold increase in mortality risk. (11)

Additionally, comorbid conditions, cardiac-specific factors, and procedural factors—as represented by Euro Score II—were significantly higher in the AKI group (3.1±1.7%). Euro Score II is a widely used risk stratification tool that has been linked to the occurrence of AKI. (12,13) Meanwhile, important procedural factors related to duration, such as CPB time, AoX time, and total surgical duration, did not differ significantly between the two groups. In this study, the underlying reason was likely the fact that the mean CPB time was less than 100 minutes. CPB time is a crucial determinant of postoperative complications—the longer the CPB time, the greater the risk of complications. A CPB time exceeding 115 minutes has been identified as an independent risk factor for AKI. (14,15)

At least two factors are associated with the PCO2 gap's preoperative elevation. A lower preoperative ejection fraction is linked to a higher PCO2 gap**,** and Euro Score II is significantly higher in patients with a preoperative PCO2 gap ≥6 mmHg. Both factors are related to the patient's preoperative cardiac condition. Since the preoperative PCO2 gap is strongly influenced by hemodynamic changes during anesthesia induction, it is suspected that myocardial depression caused by anesthetic agents contributes to an increase in the PCO2 gap.

The concept of the PCO2 gap was first introduced by Vallet et al. in 2013. This parameter has been proposed as a substitute for direct cardiac output measurement, which is often challenging due to the need for advanced equipment and operator expertise. (16) As a result, the PCO2 gap has emerged as an indirect indicator of cardiac output, offering an alternative that eliminates the variability associated with operator skill and subjective assessment using modalities such as echocardiography.

The PCO2 gap is considered a reliable marker of tissue perfusion impairment, whether due to global cardiac output reduction or microcirculatory dysfunction. (8) Under normal or hyperdynamic conditions, a normal PCO2 gap is associated with global tissue hypoxia. In these scenarios, venous blood flow is sufficient to clear the CO2 produced by hypoxic cells, even when anaerobic metabolism generates excess CO2. However, the PCO2 gap in-

creases in cases of ischemic hypoxia caused by low blood flow, while it remains unchanged in hypoxic hypoxia caused by hypoxemia. (6)

Meanwhile, an increase in the PCO2 gap ≥6 mmHg at 2 hours post-CPB is associated with higher mortality. A persistently elevated PCO2 gap correlates with poor prognosis and greater organ dysfunction, including kidney injury and death. Resuscitation strategies guided by the PCO2 gap may be beneficial for patients undergoing open-heart surgery, particularly after coming off CPB. (17-19)

Several factors following anesthesia induction contribute to myocardial depression and reduced cardiac output. However, these factors do not directly correlate with postoperative kidney injury. Instead, surgical stress, bleeding, and CPB use trigger inflammation and macro- and microcirculatory instability, leading to an elevated PCO2 gap, which is linked to organ perfusion disturbances, particularly in the kidneys.

A PCO2 gap >5.0 mmHg is a significant risk factor for the development of postoperative AKI. (6) Moreover, major postoperative complications are more common in patients with a PCO2 gap exceeding 6 mmHg. (20)

NGAL is an immunological protein in neutrophils that covalently binds to gelatinase and is present at low levels in various human tissues, including the kidneys. In cardiac surgery, NGAL is a highly specific and sensitive biomarker for detecting postoperative AKI. (21,22) Urinary NGAL levels within the first six hours following surgery increase significantly—up to 25 times the baseline value—and are markedly higher in patients who develop AKI compared to those who do not. (23)

Urinary NGAL at 2 hours post-CPB is a strong independent predictor of AKI, with an accuracy exceeding 95%. (24) Moreover, elevated NGAL levels have been used to diagnose subclinical AKI. (25) A post-CPB NGAL level >50 ng/ml indicates AKI in postoperative cardiac surgery patients. (22) Other studies suggested a cutoff of approximately 100 ng/ml, which aligned with our findings. (26) Therefore, a specific NGAL threshold at 2 hours post-CPB may serve as a reference for identifying subclinical AKI. In addition to NGAL, other sensitive biomarkers such as syndecan-1, Kim-1, interleukin-18, and serum intercellular adhesion molecule (ICAM) can also be used to assess kidney injury. (27,28)

In general, reduced cardiac output leads to an increase in venous PCO2, followed by an elevated PCO2 gap due to stasis and anaerobic metabolism. (29) In cardiac surgery, low flow, low pressure, non-pulsatile perfusion associated with CPB, hemodilution, embolism, rewarming, and intravascular hemolysis are all risk factors for renal ischemia. The kidneys also undergo anaerobic metabolism due to an imbalance between oxygen supply and demand during CPB. (30) These findings support the strong association between an elevated PCO2 gap and the incidence of postoperative AKI.

The limitation of this study is the short period of data collection, conducted over a three-month period at a single academic center. Additionally, NGAL was the only biomarker assessed in this study.

Conclusion

The PCO2 gap at 2 hours post-CPB was associated with the incidence of AKI following open-heart surgery at Dr. Wahidin Sudirohusodo Hospital, Makassar. A PCO2 gap of ≥5.7 mmHg at 2 hours post-CPB was a reliable predictor of postoperative AKI, offering a practical and operator-independent assessment. Although its accuracy is not superior to NGAL at 2 hours post-CPB, this parameter can still be used as a guideline for resuscitation during the early post-CPB phase to prevent postoperative AKI and improve patient outcomes.

Conflict of interest

We declare there is no conflict of interest in relation to this article.

Table 1. Sample characteristics related to AKI (n=22)

Variable	AKI		p
	Yes (n=8)	No (n=14)	
Age (years), mean±SD	43.63±16.76	44.29±15.26	0.926[a]
BMI (kg/m^2), mean±SD	20.94±4.03	24.20±4.09	0.086[a]
Gender, n - Male - Female	 4 4	 9 5	0.662[c]
Type of procedure, n - CABG - Valvular - Congenital	 4 3 1	 8 5 1	0.902[d]
METs, mean±SD	3.97±1.07	4.39±0.88	0.334[a]
NYHA, median (min-max)	2 (1-3)	2 (1-3)	0.364[b]
Euro score II (%), mean±SD	3.1±1.7	1.2±0.6	0.014[a]
Ejection fraction (%), mean±SD	0.49±0.15	0.57±0.09	0.574[a]
TAPSE (cm), median (min-max)	1.80 (1.0-2.0)	2.10 (1.3-2.6)	0.024[b]
Pulmonary hypertension, n - Yes - No	 3 5	 3 11	0.624[c]
Low preoperative ejection fraction (<40%), n - Yes - No	 3 5	 0 14	0.036[c]
Preoperative CVP (cmH2O), median (min-max)	11.5 (2.0-21.9)	9.3 (1.6-39.9)	0.574[b]
CVP 2 hours following off CPB (cmH2O), mean±SD	15.75±6.73	13.50±6.45	0.448[a]
AoX time (minutes), mean±SD	57.8±32.4	71.4±43.1	0.448[a]
CPB time (minutes), mean±SD	73.9±42.8	93.9±59.1	0.412[a]
Surgical duration (minutes), mean±SD	268.1±61.4	258.4±68.8	0.745[a]
Mortality <7 days, n - Yes - No	 5 3	 0 14	0.002[c]

Legend: AKI=acute kidney injury; BMI=body mass index; CABG=coronary artery bypass graft; METs=metabolic equivalents; NYHA=New York Heart Association; TAPSE=tricuspid annular plane systolic excursion; CVP=central venous pressure; CPB=cardiopulmonary bypass; AoX=aortic cross-clamp.
aIndependetnt t-test; bMann-Whitney U test; cFischer's exact test; dLikelihood ratio test.

Table 2. Sample characteristics related to preoperative PCO2 gap

Variable	Preoperative PCO2 gap (mmHg)		p
	<6	≥6	
Age (years), mean±SD	44.71±15.96	43.73±15.73	0.893[a]
BMI (kg/m^2), mean±SD	22.17±4.94	23.41±4.05	0.539[a]
Gender, n - Male - Female	 5 2	 8 7	0.648[c]
Type of procedure, n - CABG - Valvular - Congenital	 4 3 0	 8 5 2	0.436[d]
METs, mean±SD	4.68±0.29	4.03±0.97	0.138[a]
NYHA, median (min-max)	2 (1-3)	2 (1-2)	1.000[b]
Euro score II (%), mean±SD	2.42 (0.56-6.03)	1.08 (0.56-4.12)	0.021[b]
Ejection fraction (%), mean±SD	50±17	54±9	0.577[a]
TAPSE (cm), median (min-max)	1.78±0.34	1.98±0.40	0.268[a]
Pulmonary hypertension, n - Yes - No	 2 5	 4 11	1.000[c]
Low preoperative ejection fraction (<40%), n - Yes - No	 3 4	 0 15	0.023[c]
Preoperative CVP (cmH2O), median (min-max)	8.0 (2.0-39.9)	11.0 (1.6-28.0)	0.267[b]
CVP 2 hours following off CPB (cmH2O), mean±SD	12.00±4.48	15.40±7.11	0.262[a]
AoX time (minutes), mean±SD	79.6±51.48	51.5±32.5	0.294[a]
CPB time (minutes), mean±SD	97.1±64.3	81.7±49.5	0.543[a]
Surgical duration (minutes), mean±SD	276.1±73.5	255.3±62.1	0.497[a]
Mortality <7 days, n - Yes - No	 2 5	 3 12	1.000[c]

Legend: PCO2=carbon dioxide partial pressure; BMI=body mass index; CABG=coronary artery bypass graft; METs=metabolic equivalents; NYHA=New York Heart Association; TAPSE=tricuspid annular plane systolic excursion; CVP=central venous pressure; CPB=cardiopulmonary bypass; AoX=aortic cross-clamp.
[a]Independetnt t-test; [b]Mann-Whitney U test; [c]Fischer's exact test; [d]Likelihood ratio test.

Table 3. Sample characteristics related to postoperative PCO2 gap

Variable	PCO2 gap 2 hours following off CPB (mmHg)		p
	≥6	<6	
Age (years), mean±SD	43.1±16.7	44.8±15.0	0.821[a]
BMI (kg/m^2), mean±SD	22.04±4.7	23.8±3.9	0.341[a]
Gender, n - Male - Female	 5 5	 8 4	0.666[c]
Type of procedure, n - CABG - Valvular - Congenital	 5 4 1	 7 4 1	0.926[d]
METs, mean±SD	4.03±1.1	4.4±0.8	0.355[a]
NYHA, median (min-max)	2 (1-3)	1 (1-2)	1.000[b]
Euro score II (%), mean±SD	2.4±1.8	1.4±0.8	0.197[a]
Ejection fraction (%), mean±SD	50.9±13.5	54.8±10.4	0.459[a]
TAPSE (cm), median (min-max)	1.87±0.38	1.97±0.40	0.573[a]
Pulmonary hypertension, n - Yes - No	 2 8	 4 8	0.646[c]
Low preoperative ejection fraction (<40%), n - Yes - No	 3 7	 0 12	0.078[c]
Preoperative CVP (cmH2O), median (min-max)	11.5 (2.0-21.9)	9.3 (1.6-39.9)	0.872[b]
CVP 2 hours following off CPB (cmH2O), mean±SD	16.2±7.2	12.8±5.7	0.223[a]
AoX time (minutes), mean±SD	61.3±47.6	70.7±32.5	0.590[a]
CPB time (minutes), mean±SD	77.8±59.9	94.0±49.0	0.493[a]
Surgical duration (minutes), mean±SD	263.5±64.2	260.7±68.3	0.922[a]
Mortality <7 days, n - Yes - No	 5 5	 0 12	0.01[c]

Legend: PCO2=carbon dioxide partial pressure; BMI=body mass index; CABG=coronary artery bypass graft; METs=metabolic equivalents; NYHA=New York Heart Association; TAPSE=tricuspid annular plane systolic excursion; CVP=central venous pressure; CPB=cardiopulmonary bypass; AoX=aortic cross-clamp.
[a]Independetnt t-test; [b]Mann-Whitney U test; [c]Fischer's exact test; [d]Likelihood ratio test.

Table 4. Correlation between preoperative PCO2 gap with AKI

PCO2 gap (mmHg)	AKI		p
	Yes (n=8)	No (n=14)	
Preoperative, n - ≥6 - <6	 3 5	 4 10	1.000[a]
2 hours following off CPB, n - ≥6 - <6	 7 1	 3 11	0.006[a]

Legend: PCO2=carbon dioxide partial pressure; AKI=acute kidney injury; CPB=cardiopulmonary bypass.
[a]Fischer's exact test.

Table 5. Comparison between PCO2 gap and NGAL to predict AKI following open heart surgery

Variable	AKI		p	ρ	p
	Yes (n=8)	No (n=14)			
Preoperative PCO2 gap (mmHg), mean±SD	6.12±3.49	4.60±2.44	0.243[a]	0.201	0.369[b]
PCO2 gap 2 hours following off CPB (mmHg), mean±SD	7.76±2.22	4.61±2.21	0.004[a]	0.604	0.003 [b]
Preoperative NGAL (ng/ml), mean±SD	96.14±19.66	91.69±22.11	0.642[a]	0.074	0.742[b]
NGAL 2 hours following off CPB (ng/ml), mean±SD	129.18±28.81	88.88±16.26	<0.001[a]	0.700	<0.001[b]

Legend: PCO2=carbon dioxide partial pressure; NGAL=neutrophil gelatinase-associated lipocalin; AKI=acute kidney injury; CPB=cardiopulmonary bypass.
[a]Independetnt t-test; [b]Spearman correlation.

Table 6. Comparison between PCO2 gap and NGAL to predict AKI following open heart surgery

Parameters	Preoperative PCO2 gap (mmHg)	PCO2 gap 2 hours following off CPB (mmHg)	Preoperative NGAL (ng/ml)	NGAL 2 hours following off CPB (ng/ml)
AUC	62.1%	86.2%	54.5%	92%
Cut-off	5.45	5.7	100.37	100.09
Sensitivity	62.5%	87.5%	50%	87.5%
Spesivisity	57.1%	78.6%	64.3%	85.7%
PPV	45.5%	70%	44.4%	77.7%
NPV	72.3%	91.6%	69.2%	91.6%

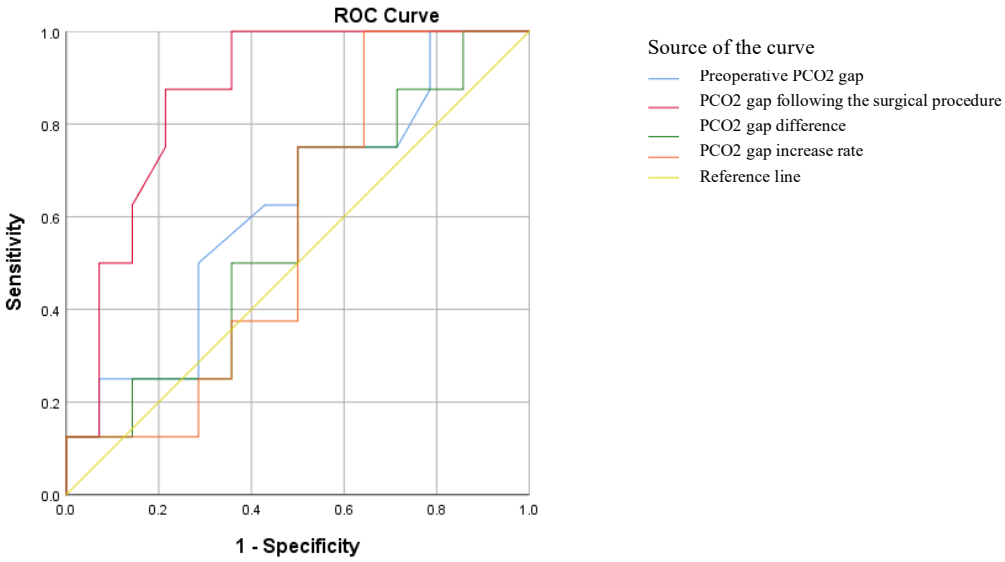
Legend: PCO2=carbon dioxide partial pressure; NGAL=neutrophil gelatinase-associated lipocalin; AKI=acute kidney injury; CPB=cardiopulmonary bypass; AUC=area under the curve; PPV=positive predictive value; NPV=negative predictive value**.**

Table 7. Comparison of accuracy between PCO2 gap and NGAL to predict AKI following open heart surgery

Parameters	AKI			p	OR	Accuracy (%)
	Yes, n (%)	No, n (%)	Total, n (%)			
PCO2 gap 2 hours following off CPB (mmHg) - ≥5.7 - <5.7	 7 (31.81%) 1 (4.55%)	 3 (13.64%) 11 (50%)	 10 (45.45%) 12 (54.55%)	 0.006	 25.6	 81.8%
NGAL 2 hours following off CPB (ng/ml) - ≥100.09 - <100.09	 7 (31.81%) 1 (4.55%)	 2 (9.09%) 12 (54.55%)	 9 (40.91%) 13 (59.09%)	 0.001	 42	 86.4%

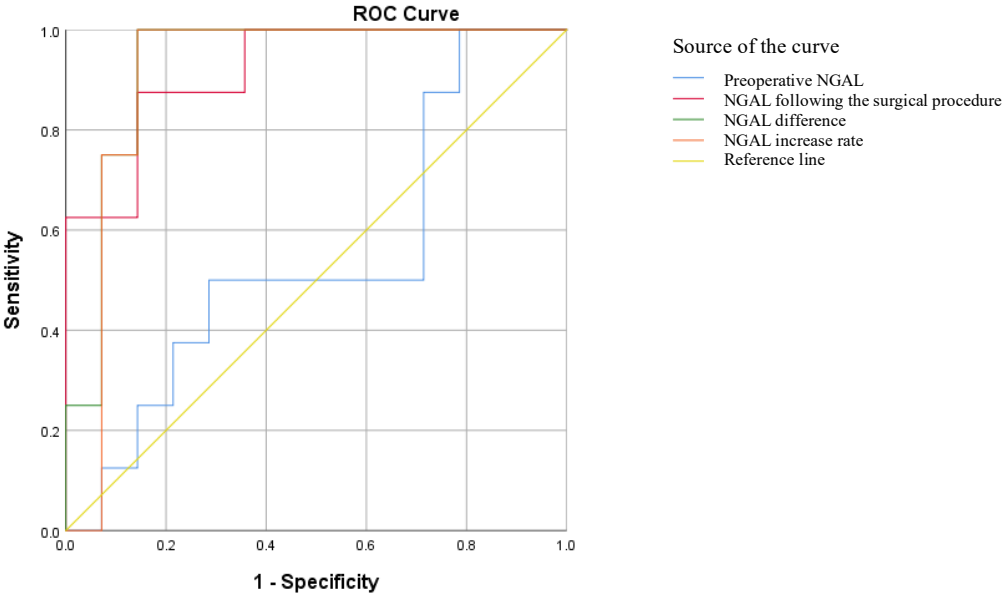
Legend: PCO2=carbon dioxide partial pressure; NGAL=neutrophil gelatinase-associated lipocalin; AKI=acute kidney injury; OR=odds ratio; CPB=cardiopulmonary bypass.

Figure 1. ROC curve of PCO2 to predict AKI following open heart surgery



Legend: ROC= receiver operating characteristic; PCO2=carbon dioxide partial pressure; AKI=acute kidney injury.

Figure 2. ROC curve of NGAL to predict AKI following open heart surgery



Legend: ROC= receiver operating characteristic; NGAL=neutrophil gelatinase-associated lipocalin; AKI=acute kidney injury.

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