ORIGINAL ARTICLE

# Plasma Neutrophil Gelatinase-Associated Lipocalin (2-0) Index: A Precise and Sensitive Predictor of Acute Kidney Injury in Children Undergoing Cardiopulmonary Bypass

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## ABSTRACT

**Objectives:** To detect the efficacy of neutrophil gelatinase-associated lipocalin (NGAL) in the early prediction of acute kidney injury (AKI) in children undergoing cardiopulmonary bypass (CPB).

**Methods:** A prospective observational study was conducted wherein 174 patients, aged 6 to 60 months, with congenital heart disease, undergoing CPB and who had a normal baseline renal function were enrolled. Plasma NGAL measurement was done preoperatively and serially at 2, 12, 24, 36, and 48 hours post-CPB initiation. Patients were classified into 2 groups according to the development of postoperative AKI.

**Results:** Plasma NGAL levels post-CPB were significantly higher in the AKI group compared to the non-AKI group with positive significant correlations between plasma NGAL level and severity of AKI. A rise in plasma NGAL of 500% from its preoperative basal level, when measured at 2 hours post-CPB initiation (NGAL 2-0 index), showed sensitivity and specificity of 83% and 64%, respectively (AUC = 0.667) and at 12 hours post-CPB initiation (NGAL 12-0 index) showed sensitivity and specificity of 66% and 64% respectively (AUC = 0.762).

**Conclusions:** Plasma NGAL is a predictive biomarker for acute kidney injury after pediatric cardiac surgery. A 500% rise in plasma NGAL at 2 hours post-CPB initiation from its basal preoperative level (NGAL 2-0 index) is a precise, sensitive, and early predictor of AKI in children.

**Keywords***: Cardiac surgery, Congenital heart disease, Dialysis, Renal failure*

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## INTRODUCTION

With rapid advances in medical care, surgeries that warrant cardiopulmonary bypass (CPB) have become increasingly common. However, CPB is a resource-intensive procedure and has been linked to an elevated risk of organ failure and mortality [1]. Acute kidney injury (AKI) poses a significant challenge in critically ill children and those undergoing cardiac surgery [1]. A multicentric epidemiological study conducted on critically ill children reported AKI in 26.9% of cases [2]; in up to 50% it developed after CPB [3-5] with 5% needing renal replacement therapy [3,6]. AKI is associated with extended stays in intensive care units and hospitals, reduced quality of life, and higher mortality rates [7,8], hence the need for timely diagnosis of AKI.

The existing diagnostic criteria for AKI primarily depend on the measurement of serum creatinine levels. However, the elevation of serum creatinine occurs late when close to 50% loss in renal function has already occurred [9]. Using plasma creatinine levels alone for assessment failed to detect AKI in 67.2% of patients with low urine output [2]. Numerous biomarkers are being investigated for their potential role in early detection of AKI. Neutrophil gelatinase-associated lipocalin (NGAL), a compact protein molecule composed of 25 units which associates with gelatinase and is secreted by neutrophils and epithelial cells, has been shown to be present in modest amounts in various organs housing epithelial tissue, such as the kidneys and lungs [10,11]. Elevated plasma NGAL levels are indicative of alterations in renal

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glomerular function and structural tubular injury, thereby enabling the early detection of AKI [12]. NGAL is being investigated for its role in early detection of AKI [13].

We conducted this study with the hypothesis that CPB leads to AKI wherein there is a predominant increase in NGAL expression within the kidneys with a minor contribution from neutrophils and other immune cells. We aimed to assess the role of sequential measurements of plasma NGAL levels (at 2 and 12 hours) following CPB in relation to the basal NGAL level (NGAL index) in the prediction of early AKI following CPB. We also examined the relationship between plasma NGAL levels and the severity of AKI.

## METHODS

We conducted a prospective observational study in the Mansoura University Children's Hospital, Mansoura, Egypt, between August 2019 and July 2023. Prior approval was obtained from the institutional ethics committee and written informed consent was obtained from the parents of all patients included in the study. Children aged 6 to 60 months with congenital heart disease undergoing CPB with a normal baseline renal function (before the procedure) adjudged on the basis of normal serum creatinine levels and adequate urine output (UOP) were included. Children with acquired heart disease or established renal impairment before the procedure were excluded from the study.

All patients included in the study were subjected to a detailed history including the reason for CPB, clinical and laboratory evaluation including serum creatinine and urine output. The type of congenital heart disease was obtained from the records. Plasma NGAL levels (25-kDa) were estimated using ELISA-based kits (Quantikine ELISA-R&D systems UK) based on sandwich ELISA principle to recognize human Lipocalin-2 [14]. NGAL levels (ng/mL) were measured immediately before initiation of CPB (0 hour) and at 2, 12, 24, 36, and 48 hours after the initiation of CPB. The percent change of plasma NGAL level at 2 and 12 hours post-CPB initiation compared to the 0 hour were calculated and were referred to as NGAL 2-0 index and NGAL 12-0 index respectively.

CPB related AKI was defined as an increase in serum creatinine of more than 1.5 fold, or a reduction in GFR of more than 25%, or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours) [15,16] occurring within 96 hours of the procedure. Duration of CPB, modified-pediatric RIFLE (pRIFLE) criteria, the worst pRIFLE score within 96 hours, length of hospital stay and the length of PICU stay were also recorded for all patients [16].

Sample size was calculated using G power program version 3.1.9.4 and on the basis of a previous study [17] that reported an effect size of 0.500 and the mean NGAL levels in those with and without AKI as 42.58 ng/dL and 36.17 ng/dL, respectively, and with a pooled standard deviation of 12.8 ng/dL. Using a 2-tailed test, type I error of 0.05 and type II error of 0.2, the total calculated sample size was 64 per group.

### Statistical analysis

Data were analyzed using SPSS version 23. Continuous variables were presented as mean (SD) while categorical variables were expressed as frequency and percentage. Independent sample t-test was used for comparing parametric continuous data between groups, and Chi square test was used for comparing groups with categorical data. Receiver operating characteristic (ROC) curves were drawn for NGAL 2-0 index and NGAL 12-0 index to assess the value of the percent change in plasma NGAL level in early discrimination of the development of AKI. Spearman correlation coefficient was used to detect the correlation between plasma NGAL level and severity of AKI (pRIFLE category). Post hoc Tukey test was used for within-group significance, and binary logistic regression was conducted to detect predictors of AKI, with estimation of adjusted odds ratio. $P$ value of $<0.05$ was considered statistically significant.

## RESULTS

We enrolled 174 children who had undergone CPB; 60 (34.5%) developed AKI while 114 (65.5%) did not develop AKI. Age, gender, nature of underlying heart disease, and 0-hour plasma NGAL level were comparable between the two groups (children with and without AKI). However, children with AKI had significantly longer CPB time, and longer duration of PICU days and longer days of hospitalization; **Table I.**

Comparison of serum NGAL levels at different points of time in AKI and non-AKI groups showed significant differences with higher levels encountered in the AKI group at 2, 12, 24, 36, and 48 hours post-CPB; **Table II.**

The 60 patients who developed AKI were further divided according to pRIFLE criteria into 24 patients (40%) with a risk of kidney injury, 18 (30%) patients with kidney injury, and 18 patients (30%) with kidney failure. A statistically significant strong positive correlation was seen between NGAL levels and severity of AKI (pRIFLE Category) at 2 hours and a moderate correlation was seen at 12 hours, 24 hours, 36 hours and 48 hours; **Table III.** We observed statistically significant positive moderate correlations between NGAL 2-0 index and NGAL 12-0

**Table I Demographic Profile of Study Population (*n* = 174)**

| | *Non-AKI (n =114)* | *AKI (n=60)* | *P value* |
|---|---|---|---|
| Age (mo)[a] | 22 (9.8) | 20.1 (6.7) | 0.141 |
| Sex[b] | | | |
| Male | 51 (44.7) | 34 (56.7) | 0.135 |
| Female | 63 (55.3) | 26 (43.3) | |
| Cardiac disease[b] | | | |
| Acyanotic | 61 (53.5) | 27 (45) | 0.286 |
| Cyanotic | 53 (46.5) | 33 (55) | |
| Preoperative Plasma NGAL (ng/mL)[a] | 46.5 (4.4) | 46.1 (5.5) | 0.618 |
| Cardio-pulmonary bypass time (min)[a] | 115.5 (10.6) | 156.8 (15.6) | 0.001 |
| Length of hospital stay (d)[a] | 6.3 (1.7) | 18.4 (3.8) | 0.001 |
| Length of PICU stay (d)[a] | 3.3 (1.2) | 11.5 (3.9) | 0.001 |

*Data expressed as [a]mean (SD) or [b]n (%). AKI Acute kidney injury, NGAL Neutrophil gelatinase-associated lipocalin*

**Table II Comparison of Plasma Neutrophil Gelatinase-Associated Lipocalin (ng/mL) Levels at Different Points of Time Post-cardiopulmonary Bypass Initiation in AKI and Non-AKI Groups (pRIFLE Category)**

| *Time* | *Non-AKI (n = 114)* | *AKI (n = 60)* | *P value* |
|---|---|---|---|
| 0 h | 46.5 (4.4) | 46.1 (5.5) | 0.618 |
| 2 h | 87.9 (19.6) | 275.2 (44.8) | < 0.001 |
| 12 h | 84.2 (23.6) | 268.3 (70.2) | < 0.001 |
| 24 h | 79.8 (25.8) | 303.5 (90.2) | < 0.001 |
| 36 h | 76.5 (22.5) | 277.7 (95.7) | < 0.001 |
| 48 h | 71.8 (26.2) | 222.7 (83.4) | < 0.001 |

*AKI Acute kidney injury. Data expressed as mean (SD)*

index with the severity of AKI (pRIFLE category) in children who developed AKI; **Table IV.**

For NGAL 2-0 index, sensitivity and specificity were 83% and 64% respectively at a 500% rise in plasma NGAL from its basal level with an area under the curve (AUC, 95% CI) of 0.667 (0.515-0.818), *P* = 0.042, positive predictive value (PPV) 45.5%, negative predictive value (NPV) 88.9%, positive likelihood ratio (LR) 2.3 and negative LR 0.266 (**Fig. 1a**). Moreover, a rise of NGAL 12-0 index of 500% had a sensitivity and specificity of 66% and 64% respectively with an AUC (95% CI) of 0.762 (0.641-0.883), *P* = 0.001, PPV 40%, NPV 80%, positive LR 1.7 and negative LR 1.88 (**Fig 1b**). While comparing the AUC for NGAL 2-0 index and NGAL 12-0 index *P* value for the difference between them was 0.482**.**

Binomial regression analysis with odds ratio for NGAL 2-0 index and 12-0 index showed overall percentage correctly classified as AKI as 94.8%, model $\chi^2 = 183.16$, $P < 0.001$, Nagelkerke $R^2 = 0.85$; **Table V.**

## DISCUSSION

Cardiopulmonary bypass surgery is recognized as one of the most frequently conducted major surgical procedures on a global scale [18]. Within this context, AKI poses a significant and frequent complication which is associated with a high mortality rate [19]. In our study, the incidence rate of AKI after CPB surgery was almost 34.5%. We also observed increased levels of NGAL in AKI patients; this was in concordance with the results of previous studies [5,17,20]. A study by Fadel and colleagues showed a significant difference in plasma NGAL between the AKI group and the non-AKI group at 2, 12, and 24 hours post-CPB [17].

In 2023, a meta-analysis by Zou et al examined the predictive value of NGAL for AKI in pediatric cases. The

**Table III Correlations between Plasma NGAL levels (ng/ml) at different points of time post-CPB initiation and severity of AKI (pRIFLE category) (*n* = 60)**

| | *Plasma NGAL* | | | | |
|---|---|---|---|---|---|
| | 2 hrs | 12 hrs | 24 hrs | 36 hrs | 48 hrs |
| Risk (*n* = 24) | 241.1 (45.9)[a,b] | 229.3 (64.5)[a] | 246 (96)[a,b] | 238.7 (102.7)[a] | 170.8 (71.6)[a,b] |
| Injury (*n* =18) | 289.8 (29.8)[a] | 256 (49.1)[b] | 321 (43)[a] | 263.1 (29.7)[b] | 249.6 (71.5)[a] |
| Failure (*n* =18) | 306.1 (18.3)[b] | 332.5 (48.8)[a,b] | 362.6 (72.6)[b] | 344.4 (97.8)[a,b] | 264.9 (75.2)[b] |
| *r* | 0.65 | 0.55 | 0.53 | 0.45 | 0.45 |
| *P* value | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| $R^2$ | 0.388 | 0.363 | 0.300 | 0.204 | 0.237 |

*AKI acute kidney injury, CPB Cardiopulmonary bypass, NGAL Neutrophil gelatinase-associated lipocalin. Data expressed as mean (SD), r Spearman correlation coefficient, $R^2$ Coefficient of determination. Similar superscripted letters denote significant difference within the same column by post-hoc Tukey test*

**Table IV Correlations Between Percent Change in Plasma NGAL Level at different Points of Time Post-CPB Initiation and Severity of AKI (pRIFLE category) in Patients who Developed AKI (*n* = 60)**

| | *NGAL 2-0 index* | *NGAL 12-0 index* |
|---|---|---|
| Risk (*n* = 24) | 450 (130)$^{a,b}$ | 420 (150)$^{a}$ |
| Injury (*n* = 18) | 530 (110)$^{a}$ | 450 (80)$^{b}$ |
| Failure (*n* = 18) | 540 (90)$^{b}$ | 600 (140)$^{a,b}$ |
| r | 0.37 | 0.42 |
| *P* value | 0.004 | 0.001 |
| $R^2$ | 0.386 | 0.363 |

*NGAL: Neutrophil gelatinase-associated lipocalin; CPB: Cardiopulmonary bypass; AKI acute kidney injury*
*Data expressed as mean percent (SD), r Spearman correlation coefficient, $R^2$ Coefficient of determination*
*Similar superscripted letters denote significant difference within same column by Post Hoc Tukey test*

**Table V Binomial Regression Analysis for Plasma NGAL Levels at Different Points of Time Post-CBP Initiation (NGAL 2-0 and NGAL 12-0 indices)**

| | *β* | *P value* | *aOR (95% CI)* |
|---|---|---|---|
| NGAL-2-0 index | 0.984 | 0.04* | 2.67 (1.08, 7.85) |
| NGAL-12-0 index | 0.064 | < 0.001* | 1.07 (1.04, 1.09) |

*Overall percentage correctly classified 94.8%*
*Model $\chi^2 = 183.16$*
*P < 0.001**
*Nagelkerke $R^2 = 0.85$*

*aOR Adjusted odds ratio, CPB Cardiopulmonary bypass, NGAL Neutrophil gelatinase-associated lipocalin*

analysis included 5,049 patients, with 1,861 diagnosed with AKI. Among them, 15 studies focused on AKI after CPB surgery. The findings suggest NGAL is predictive of AKI across diverse contexts in children, with no significant difference in predictive accuracy between urine and blood measurements [1].

Unlike our study, a study by Parikh et al found limited predictive capacity for AKI in children using plasma NGAL. The reason may be that patients labeled as "non-AKI" showed higher postoperative plasma NGAL elevations than in previous studies, resulting in relatively small differences in NGAL concentrations between AKI and non-AKI groups. This discrepancy may be due to variations in the assay used to measure plasma NGAL [21].

In our study, there were statistically significant positive correlations between plasma NGAL levels post-CPB initiation and the severity of AKI (pRIFLE category). This indicates that plasma NGAL rises with worsening renal function. Previous studies also found a positive correlation between plasma NGAL and AKI severity assessed using serum creatinine rather than pRIFLE categorization [17,20,22]. This finding is consistent with another study in adults [23].

However, on a contrasting note, Ricci et al did not accurately predict AKI diagnosis (pRIFLE classification0 using NGAL levels. This may be due to NGAL levels being measured only once per patient, within one hour of admission to the ICU after surgery [6]. Similar findings were reported by Koch et al where single NGAL measurements within 30 minutes of ICU admission led to inconsistent results [24].

We would recommend NGAL 2-0 index over NGAL 12-0 index despite no significant difference between their AUC, and NGAL 2-0 can predict AKI earlier. The recent

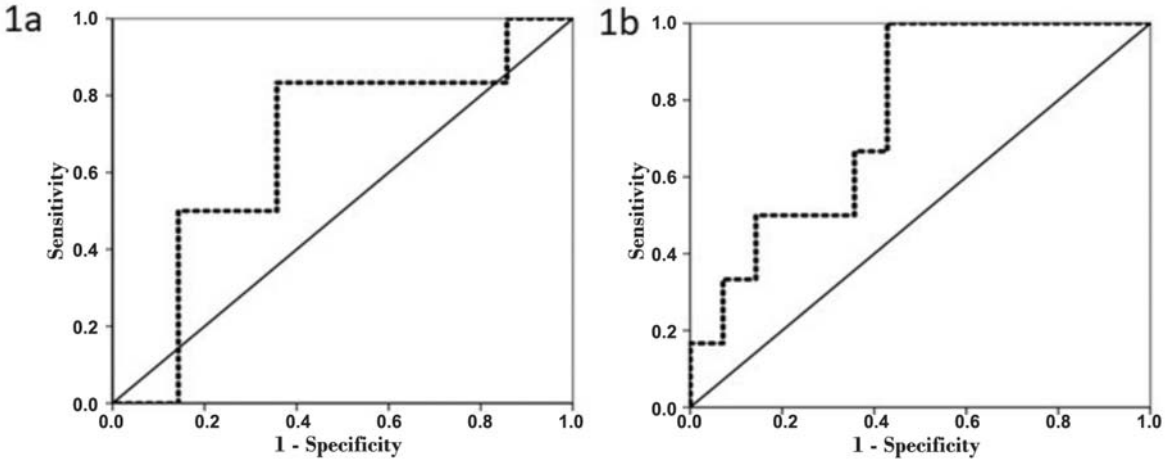


**Fig. 1** Receiver operating characteristic (ROC) curve for **(a)** NGAL 2-0 index, **(b)** NGAL 12-0 index

**WHAT THIS STUDY ADDS?**

- A percent rise in the plasma NGAL at 2 hours (NGAL 2-0 index) is a reasonable predictor for acute kidney injury in children undergoing cardiopulmonary bypass.
- Plasma NGAL levels correlate with the severity of acute kidney injury.

meta-analysis agreed with our preference and concluded that plasma NGAL at 2 hours was more sensitive and specific than 12 hours [1].

Most pediatric studies showed a high sensitivity and specificity of NGAL at different times post-CPB, however, they determined the cut-off level at one point with the highest accuracy [5,17,20]. However, our study calculated the percent change in plasma NGAL between two points. We assumed that this observation may help patients with pre-existing renal disease undergoing cardiac surgery if they have a higher basal level of NGAL, but this should be validated by further studies.

A significant difference was observed in CPB duration, hospital stay, and PICU stay between the AKI and non-AKI groups. Longer CPB duration correlated with increased complications as also seen in some studies [5,20] but refuted in a study by Ricci et al [6].

To our knowledge, this is the first study in children that evaluated the intraoperative plasma NGAL levels. Our methodology was based on research by Friedrich et al in Germany, who pioneered the evaluation of intraoperative urinary NGAL [25] and found that urinary NGAL levels at 2 hours postoperation were significantly elevated compared to preoperative values ($P < 0.01$), with a mean CPB duration of 141 minutes.

Our study holds several noteworthy strengths. Firstly, it is a prospective recruitment of pediatric patients and minimal confounding factors unlike adult studies where results may be confounded by underlying diabetes mellitus and hypertension. All participants in our study had normal baseline kidney function facilitating a precise understanding of how plasma NGAL levels correlate with subsequent changes in serum creatinine. We utilized a plasma biomarker instead of a urinary one, overcoming limitations associated with urinary biomarkers such as the absence of samples from severely oliguric patients and the influence of hydration and diuretics on urinary biomarker concentrations. We recorded serial plasma NGAL estimates at different time points starting from the initiation of CPB surgery rather than a single record at the end of the surgery or ICU admission, providing insights into the duration and complexity of surgery affecting the development of AKI. Further, we calculated the NGAL index and percent change of plasma NGAL between time points instead of relying on a cut-off value, enhancing sensitivity and specificity in predicting AKI.

Our study has some limitations. such as children under 6 months of age were not included, and the cohort was heterogeneous, including both cyanotic and acyanotic congenital heart diseases without risk adjustment for congenital heart surgery. Confounding variables such as inotropic support were not accounted for which could impact AKI incidence alongside CPB duration. Additionally, combining multiple biomarkers is recommended to provide a more thorough panel for early AKI diagnosis.

We conclude that AKI is a common and significant complication following CPB procedures. Plasma NGAL 2-0 index can serve as an early predictive biomarker for AKI and correlates with the AKI severity.

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## REFERENCES

1. Zou Z, Chen B, Tang F, et al. Predictive value of neutrophil gelatinase-associated lipocalin in children with acute kidney injury: A systematic review and meta-analysis. Front Pediatr. 2023;11:1147033.
2. Kaddourah A, Basu RK, Bagshaw SM, et al. Epidemiology of acute kidney injury in critically ill children and young adults. N Engl J Med. 2017;376:11-20.
3. Bennett M, Dent CL, Ma Q, et al. Urine NGAL Predicts severity of acute kidney injury after cardiac surgery: A prospective study. Clin J Am Soc Nephrol. 2008;3:665-73.
4. Zheng J, Xiao Y, Yao Y, et al. Comparison of urinary biomarkers for early detection of acute kidney injury after cardiopulmonary bypass surgery in infants and young children. Pediatr Cardiol. 2013;34:880-6.
5. Krawczeski CD, Woo JG, Wang Y, et al. Neutrophil gelatinase-associated lipocalin concentrations predict development of acute kidney injury in neonates and children

after cardiopulmonary bypass. J Pediatr. 2011;158:1009-15.e1.
6. Ricci Z, Netto R, Garisto C, et al. Whole blood assessment of neutrophil gelatinase-associated lipocalin versus pediatric RIFLE for acute kidney injury diagnosis and prognosis after pediatric cardiac surgery: Cross-sectional study. Pediatr Crit Care Med. 2012;13:667-70.
7. Sterling M, Al-Ismaili Z, McMahon KR, et al. Urine biomarkers of acute kidney injury in noncritically ill, hospitalized children treated with chemotherapy. Pediatr Blood Cancer. 2017;64:10.1002/pbc.26538.
8. Afify MF, Maher SE, Ibrahim NM, et al. Serum neutrophil gelatinase-associated lipocalin in infants and children with sepsis-related conditions with or without acute renal dysfunction. Clin Med Insights Pediatr. 2016;10:85-9.
9. Jayaraman R, Sunder S, Sathi S, et al. Post cardiac surgery acute kidney injury: A woebegone status rejuvenated by the novel biomarkers. Nephrourol Mon. 2014;6:e19598.
10. Albert C, Zapf A, Haase M, et al. Neutrophil gelatinase-associated lipocalin measured on clinical laboratory platforms for the prediction of acute kidney injury and the associated need for dialysis therapy: A systematic review and meta-analysis. Am J Kidney Dis. 2020;76:826-41.e1.
11. Moledina DG, Parikh CR, Garg AX, et al. Association of perioperative plasma neutrophil gelatinase-associated lipocalin levels with 3-year mortality after cardiac surgery: A prospective observational cohort study. PLoS One. 2015;10:e0129619.
12. Kališnik JM, Hrovat E, Hrastovec A, et al. Creatinine, neutrophil gelatinase-associated lipocalin, and cystatin c in determining acute kidney injury after heart operations using cardiopulmonary bypass. Artif Organs. 2017;41:481-9.
13. Liu X, Guan Y, Xu S, et al. Early predictors of acute kidney injury: A Narrative review. Kidney Blood Press Res. 2016;41:680-700.
14. Rampoldi B, Tessarolo S, Giubbilini P, et al. Neutrophil gelatinase-associated lipocalin and acute kidney injury in endovascular aneurysm repair or open aortic repair: A pilot study. Biochem Med (Zagreb). 2018;28:010904.
15. Bellomo R, Ronco C, Kellum JA, et al. Acute Renal Failure - Definition, Outcome Measures, Animal Models, Fluid Therapy and Information Technology Needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004;8:R204-12.
16. Akcan-Arikan A, Zappitelli M, Loftis LL, et al. Modified RIFLE criteria in critically ill children with acute kidney injury. Kidney Int. 2007;71:1028-35.
17. Fadel FI, Abdel Rahman AM, Mohamed MF, et al. Plasma neutrophil gelatinase-associated lipocalin as an early biomarker for prediction of acute kidney injury after cardio-pulmonary bypass in pediatric cardiac surgery. Arch Med Sci. 2012;8:250-5.
18. Galiæ S, Miloševiæ D, Filipoviæ-Grèiæ B, et al. Early biochemical markers in the assessment of acute kidney injury in children after cardiac surgery. Ther Apher Dial. 2022;26:583-93.
19. Chertow GM, Levy EM, Hammermeister KE, et al. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med. 1998;104: 343-8.
20. Dent CL, Ma Q, Dastrala S, et al. Plasma neutrophil gelatinase-associated lipocalin predicts acute kidney injury, morbidity and mortality after pediatric cardiac surgery: a prospective uncontrolled cohort study. Crit Care. 2007;11:R127.
21. Parikh CR, Devarajan P, Zappitelli M, et al. Postoperative biomarkers predict acute kidney injury and poor outcomes after pediatric cardiac surgery. J Am Soc Nephrol. 2011;22:1737-47.
22. Peco-Antiæ A, Ivaniševiæ I, Vuliæeviæ I, et al. Biomarkers of acute kidney injury in pediatric cardiac surgery. Clin Biochem. 2013;46:1244-51.
23. de Geus HR, Bakker J, Lesaffre EM, et al. Neutrophil gelatinase-associated lipocalin at ICU admission predicts for acute kidney injury in adult patients. Am J Respir Crit Care Med. 2011;183:907-14.
24. Koch AM, Dittrich S, Cesnjevar R, et al. Plasma neutrophil gelatinase-associated lipocalin measured in consecutive patients after congenital heart surgery using point-of-care technology. Interact Cardiovasc Thorac Surg. 2011;13:133-6.
25. Friedrich MG, Bougioukas I, Kolle J, et al. NGAL expression during cardiopulmonary bypass does not predict severity of postoperative acute kidney injury. BMC Nephrol. 2017;18:73.