# Monocyte to Lymphocyte Ratio, A Novel Predictor of Acute Kidney Injury After Cardiac Valve Surgery

Zhenhua Wang, MD,<sup>1,2</sup> Jialiang Li, MD,<sup>3</sup> Han Song, MD,<sup>1,2</sup> Duoliang Wei, MD,<sup>1,2</sup> Xin Zhao, MD, PhD<sup>1,2</sup>

<sup>1</sup>Department of Cardiovascular Surgery, Qilu Hospital of Shandong University, No. 107 West Wenhua Road, Jinan, Shandong, China; <sup>2</sup>Institute of Thoracoscopy in Cardiac Surgery, Shandong, China

<sup>3</sup>Department of Vascular Surgery, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

## ABSTRACT

**Background**: Although inflammation contributes to the development of acute kidney injury (AKI), the role of monocyte to lymphocyte ratio (MLR) in predicting the risk of post-operative AKI in patients underwent cardiac surgery is not completely clear yet. This study aimed to investigate whether elevated MLR predicts postoperative AKI.

**Materials and methods**: In this retrospective study, a total of 331 adult patients who underwent heart valve replacement were included. These patients are not distinguished between single valve replacement or double valve replacement. AKI was diagnosed, according to the KDIGO classification criteria. The associations between monocyte to lymphocyte ratio (MLR), neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) and the occurrence of AKI were investigated.

**Results:** Postoperative AKI was detected in 37 (11.2%) patients. In the early period after surgery, the patients who developed AKI had a significant higher preoperative MLR than those who did not (0.38(0.33-0.44) vs. 0.26(0.20-0.34), = 0.02). The receiver operating characteristics (ROC) curve showed that the area under the curve (AUC) of the MLR for predicting AKI was 0.772 (P = 0.01), and the cut-off value was 0.47. Multivariate logistic regression analysis suggested that the higher preoperative MLR ( $\geq$ 0.47) was independent predictor of AKI (OR: 2.951, 95% CI: 1.412-6.167, P = 0.004). According to the cut-off value group verification, patients in the higher preoperative MLR group are more likely to have low cardiac output syndrome (LCOS), renal replacement therapy, and hospital death after surgery.

**Conclusion**: These results showed that MLR could be used as a cost-effective predictor of postoperative AKI in patients who undergo heart valve replacement surgery.

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## INTRODUCTION

Valvular heart disease (VHD) is a disease in which the function of the leaflets is progressively reduced by genetic or environmental factors. VHD still is one of the most important types of cardiovascular diseases in cardiac surgery. Up to now, heart valve replacement surgery is the main treatment in reducing patient mortality and improving patients' quality of life [Nishimura 2017]. However, cardiac surgery is associated with high risk and postoperative complications. Among them, acute kidney injury (AKI) is the most common clinically important complication in patients undergoing open heart surgery and is associated with increased mortality and morbidity [Wang 2017]. The incidence of AKI varies from 4% and 42%, and it is associated with 3-8-fold higher perioperative mortality [Hobson 2009]. Nevertheless, besides clinical features, there are few preoperative prognostic markers available, including glutathione transferase- $\varpi$ , urinary  $\alpha$ 1 microglobulin, N-acetylβ-d-glucosaminidase, serum and urinary neutrophil gelatinase-associated lipocalin [Prowle 2015]. However, the applicability and validity of these markers to a broad population of patients undergoing cardiac surgery still are uncertain.

Preoperative systemic inflammatory markers easily can be measured with a routine blood sample, are inexpensive, and their value in predicting kidney dysfunction has been described [Chen 2019]. The main systemic inflammatory markers include monocyte to lymphocyte ratio (MLR), neutrophil to lymphocyte ratio (NLR), and platelet to lymphocyte ratio (PLR). However, little is known about the value of these markers in risk of postoperative AKI. Therefore, the current study aimed to identify whether these markers are prognostic in patients undergoing heart valve replacement surgery for postoperative AKI.

# MATERIALS AND METHODS

**Subjects**: In this retrospective analysis, we collected 331 patients from the Qilu Hospital of Shandong University who underwent elective heart valve surgery between December 2016 and December 2018. The study was approved by the Ethics Committee of Qilu Hospital, Shandong University. The need for informed consents were waived because the study was noninterventionally designed, and the data was

Correspondence: Xin Zhao, MD, PbD, Qilu Hospital, Shandong University, No.107, Wen Hua Xi Road, Jinan, Shandong, 250012, P.R. China, Telephone 18560086772 (e-mail: zhaoxin@email.sdu.edu.cn).

anonymous.

**Inclusion and exclusion criteria**: The inclusion criteria were adult patients (age≥18 years) who underwent open heart surgery due to valvular heart disease, without aortic or coronary artery-related surgery. There is no history of chronic kidney disease or kidney surgery, and no history of renal replacement therapy (RRT). Exclusion criteria were patients

with aortic or coronary artery disease requiring surgical treatment, severe heart failure (NYHA-III and NYHA-IV), infective endocarditis, hematopoietic disease, liver or renal dysfunction, stroke, tumor, thyroid disease, autoimmune disease, and infectious diseases.

**Baseline variables collection**: We conducted the study based on the electronic data capture and analysis system for

## Table 1. Demographics and baseline data in the two groups

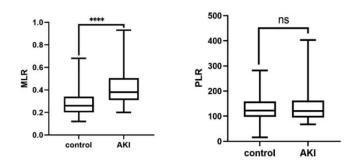
	Total	Control group ( <i>N</i> = 294)	AKI group ( <i>N</i> = 37)	P-value
Clinical characteristics				
Age (years)	58 (51-64)	58 (50-64)	61 (53-67)	0.08
Weight (kg)	65 (58-74)	65 (58-74)	70 (60-76)	0.15
Hospitalization expenses (yuan)	135489 (116135-164995)	133975 (115695-162440)	154379 (127478-187878)	0.01
Gender (male/female, n)	203/128	176/118	44496	0.12
Diabetes, n (%)	24 (7.3)	22 (7.5)	2 (5.4)	0.65
Hypertension, n (%)	107 (32.3)	93 (31.6)	14 (37.8)	0.45
CAD, n (%)	59 (17.8)	52 (17.7)	7 (18.9)	0.85
Smoking, n (%)	107 (32.3)	97 (33.3)	10 (27)	0.47
Drinking, n (%)	110 (33.2)	101 (34.4)	9 (24.3)	0.22
ACEI/ARB, n (%)	38 (11.5)	33 (11.5)	5 (13.5)	0.27
Furosemide, n (%)	207 (62.5)	185 (62.9)	22 (59.5)	0.68
Spironolactone, n (%)	252 (76.1)	223 (75.9)	29 (78.4)	0.73
Operation time (min)	285 (240-340)	280 (240-334.3)	300 (255-375)	0.06
CPB time (min)	234 (154-309)	231 (152-309)	243 (175-350)	0.09
.A (mm)	40 (34-47)	40 (33-46)	46 (37-53)	0.00
.V (mm)	46 (41-52)	46 (41-52)	46 (41-51)	0.86
.VEF (%)	0.58 (0.53-0.62)	0.58 (0.52-0.62)	0.57 (0.53-0.62)	0.89
aboratory characteristics				
WBC (10 <sup>9</sup> /L)	5.81 (4.86-6.98)	5.82 (4.85-6.94)	5.56 (4.92-7.42)	0.89
Neutrophil (10 <sup>9</sup> /L)	3.32 (2.74-4.35)	3.32 (2.73-4.30)	3.32 (2.80-4.76)	0.68
ymphocyte (10º/L)	1.69 (1.33-2.10)	1.70 (1.35-2.09)	1.65 (1.24-2.15)	0.34
Monocyte (10 <sup>9</sup> /L)	0.46 (0.38-0.54)	0.45 (0.37-0.53)	0.53 (0.45-0.69)	0.04
RBC (10 <sup>12</sup> /L)	4.63 (4.27-4.94)	4.61 (4.27-4.94)	4.73 (4.28-5.15)	0.92
Platelet (10 <sup>9</sup> /L)	210 (175-254)	211 (178-256)	199 (168-241)	0.47
Creatinine (µmol/L)	72 (60-88)	70 (58-83)	71 (61-86)	0.01
Jric Acid (µmol/L)	327 (273-405)	325 (271-404)	349 (281-407)	0.09
RBC transfusion (u)	4 (4-6)	4 (4-6)	4 (4-7)	0.40
Plasma transfusion (ml)	400 (400-600)	400 (400-600)	400 (400-600)	0.24
MLR (%)	0.27 (0.21-0.36)	0.26 (0.20-0.34)	0.38 (0.33-0.44)	0.02
NLR (%)	2.00 (1.57-2.50)	1.98 (1.56-2.46)	2.16 (1.57-2.65)	0.14
PLR (%)	124 (96.90-158)	124 (97-159)	120 (97-156)	0.88

CAD, coronary artery disease; ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers; CPB, cardiopulmonary bypass; LA, left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; WBC, white blood cell; RBC, red blood cell; MLR, monocyte to lymphocyte ratio; NLR, neutro-phil to lymphocyte ratio; PLR, platelet to lymphocyte ratio

each included patient. Demographic characteristics, comorbidities, laboratory test results, and postoperative blood transfusion were collected. Blood routine was tested on an empty stomach in the morning of the second day after admission and the counts of monocyte, lymphocyte, neutrophil, and platelet were obtained. MLR, NLR, and PLR were calculated. The preoperative serum creatinine (Cr) measurements basically were close to steady state. The renal function analysis test was performed on the first postoperative day. After discharge, renal function was checked once every three months. Hypertension was defined as a self-reported history or the use of antihypertensive drugs, or the average of two resting systolic blood pressure readings of ≥140 mmHg and/ or diastolic blood pressure≥90mmHg [James 2014]. Diabetes mellitus was defined as a self-reported history of diabetes, or fasting blood glucose≥7.0 mmol/L or the use of insulin and/or oral hypoglycemic medications [Association 2013]. History of coronary artery disease (CAD) was defined as a physician's diagnosis of CAD, prior myocardial infarction, or coronary revascularization (percutaneous coronary intervention or coronary artery bypass graft) [Joodi 2019].

**Definition of AKI**: According to the common diagnostic criteria for KDIGO criteria, AKI was defined as serum Cr increased ≥26.5 umol/L (0.3mg/dl) in 48h or 1.5 times from the baseline within 7 days [Kellum 2012].

**Statistical analyses:** Continuous normally distributed variables are expressed as mean ± standard deviation, variables of continuous skewness distribution are expressed as the



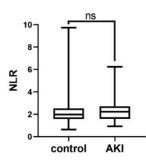


Figure 1. Box plot of differences between groups of new inflammatory response markers

median and interquartile range, and the categorical data is expressed in numbers and percentages. According to changes in serum Cr, patients were divided into two groups: control group and AKI group. Analyzing continuous variables by independent Student's t test or Mann-Whitney U test. Using  $\chi^2$  test or Fisher's exact test to analyze categorical variables. The statistically significant variables in the univariate analysis were included in the multivariate logistic regression analysis to evaluate the risk factors for postoperative AKI. The receiver operating characteristic (ROC) curve is used to derive the sensitivity and specificity of each systemic inflammation index to predict the risk of AKI. Youden's J statistic (sensitivity + specificity -1) is used to determine the best cutoff value for each systemic inflammation index. *P* < 0.05 was considered statistically significant.

### RESULTS

Baseline characteristics: In total, 331 patients (203/128, male/female, mean age 58 (51-64) years) undergoing elective heart valve surgery were enrolled in our present study. Thirty-seven (11.2%) patients developed postoperative AKI, based on the KDIGO criteria. Baseline data includes age, body weight, LVEF, LV, operation time, CPB time, WBC, RBC, neutrophil, lymphocyte, platelet, uric acid, RBC and plasma transfusion, NLR and PLR were not significantly different between the control and the AKI groups (P < 0.05). This shows that there is a good balance between the baseline data and preoperative treatment measures between the two groups. The history of smoking and drinking, comorbidities of hypertension, CAD, diabetes, preoperative drugs application and postoperative complications, including pneumonia and severe arrhythmia, were similarly indistinguishable between the two groups (P < 0.05). The monocyte count (0.53 vs. 0.45\*109/L, P = 0.00), MLR (0.38 vs. 0.26, P = 0.02), left atrium (46 vs. 40, P = 0.00), and hospitalization expense (133975 vs. 154379 -yuan, P = 0.01) of the AKI group were significantly higher than that in the control group. (Table 1)

At the same time, GraphPad Prism 8 software was used to draw box plots of three new inflammatory response markers, indicating that MLR has good statistical significance. (Figure 1)

**Predictive effect of MLR and monocyte number**: Because the cut-off values of MLR and monocyte number used for prognostication in AKI are lacking in previous studies, we performed cut-off optimization for MLR and monocyte number in our study. We first assessed the impact of MLR on the risk of postoperative AKI. Cut-off points of 0.47 revealed the highest Youden value to risk of postoperative AKI in ROC curve. Thus, we used 0.47 to divide the patients in to two categories. The cut-off value of 0.47 significantly predicts postoperative AKI risk at 89.2% sensitivity and 58.2% specificity with and the area under the curve (AUC) of 0.772 (Figure 2A). (Figure 2)

Then, we observed the prognostic value of monocyte number. The cut-off point of 0.43 exhibited the highest Youden value to postoperative AKI using ROC curve. Thus, we used 0.43 to divide patients into two groups. The cut-off value of 0.43 significantly predicts postoperative AKI risk at 78.4% sensitivity and 56.8% specificity with and AUC of 0.719 (Figure 2B).

Comparison of the AKI incidence by MLR and monocyte number categories: The occurrence rate of AKI was higher in the high MLR group as compared with the low MLR group (21.4% vs. 6.8%, P = 0.002). In addition, high monocyte number also showed a higher AKI incidence compared with the low number group (17.4% vs. 6.3%, P =0.013). (Table 2)

**Multivariate regression analysis:** Incorporating the positive indicators of univariate analysis into multivariate logistic regression analysis, the results showed that the higher preoperative MLR (OR: 2.951,95% CI: 1.412-6.167, P = 0.00) and monocyte number (OR: 2.567, 95% CI: 1.128-5.864, P =0.03) were associated with postoperative AKI. (Table 3)

Incidence of postoperative complications in different grades of MLR group: The short-term postoperative complications rates of patients were verified into two groups, according to the best cut-off value of MLR, including low cardiac output syndrome, postoperative renal replacement therapy application, severe arrhythmia, and hospital death. Severe arrhythmia manifested as atrial fibrillation, supraventricular tachycardia, multiple ventricular premature beats, ventricular tachycardia, ventricular fibrillation, etc. The results show that patients in the high MLR group are more likely to have postoperative low cardiac output syndrome (13.4% vs. 3.7%, P = 0.00), more possibility to accept renal replacement therapy (1.1% vs. 5.6%, P = 0.02), and higher in-hospital mortality (1.6% vs. 5.6%, P = 0.04). (Table 4)

#### DISCUSSION

AKI is a serious adverse event after cardiac surgery and is associated with long-term sequelae, healthcare costs, and a high rate of death. Inflammation plays an important role in the initiation and progression of AKI [Rabb 2016]. MLR, NLR, and PLR are the main markers of systematic inflammation. They are combined by the count ratio between the white blood cell subtypes, which are more balanced and stable than a single subtype. The body's inflammatory changes and inflammatory state are clinically easy to obtain and widely have been used in clinics. They have been used in malignant tumors, coronary heart disease, atrial fibrillation, and other studies have shown value in diagnosis and treatment. More and more clinical evidence shows that systemic inflammation markers play an important role in the development of AKI in the current study. We evaluated the independent predictive value of MLR, NLR, and PLR for postoperative AKI in patients who underwent heart valve surgery and found that high MLR was associated with remarkably increased postoperative AKI risk.

Postoperative AKI is a syndrome with a wide range of causes and cause serious complications [Bellomo 2008]. To date, the pathophysiology of cardiac surgery-associated AKI remains poorly understood [Ronco 2019]. Given the short and long-term impact of postoperative AKI, it is highly important to detect markers and early markers of AKI in order to timely prevent and treat this complication [Romagnoli 2018].

Table 2. Comparison of the AKI incidence by MLR and monocyte number categories

	AKI	Not AKI	Р
MLR<0.47 (N = 189)	12	177	0.002
MLR≥0.47 ( <i>N</i> = 142)	25	117	
Monocyte<0.43(109/L) (N = 135)	8	127	0.013
Monocyte≥0.43(109/L) (N = 196)	29	167	

AKI, acute kidney injury; MLR, monocyte to lymphocyte ratio

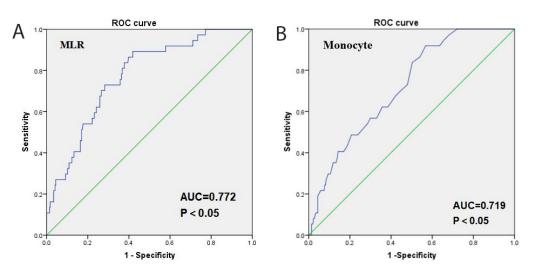


Figure 2. ROC curve analyses of monocyte to lymphocyte ratio (MLR), monocyte number and postoperative acute kidney injury (AKI). A) ROC curve of MLR; B) ROC curve of monocyte number.

Biomarkers of kidney injury are new tools for risk assessment and could possibly improve therapy. Although recent studies have shown that Neutrophil Gelatinase-Associated Lipocalin (NGAL), tissue inhibitor of metalloproteinases 2 (TIMP-2), insulin-like growth factor binding protein 7 (IGFBP7), urine Regulatory protein (UMOD), matrix metalloproteinase 7 (MMP-7), glutathione transferase- $\varpi$ , urinary  $\alpha$ 1 microglobulin, N-acetyl $\beta$ -d-glucosaminidase and other biomarkers are associated with cardiac surgery AKI [Wu 2019], but they are expensive, and it is not easy to apply to a wide range of patient groups.

Accumulating clinical evidence show that systematic inflammatory markers play an important role in the development of AKI [Bonavia 2018; Fani 2018]. Recently, NLR has been reported to be a reliable biomarker for the early detection of AKI [Chen 2019]. Another study found that the preoperative PLR was associated in a U-shaped pattern with survival among patients with AKI [Zheng 2017]. Gameiro et al. found that the neutrophils to lymphocytes and platelets ratio was independently associated with AKI after abdominal surgery, although there was no association with in-hospital mortality [Gameiro 2018]. Very recently, Zhang et al. reported that MLR was associated with the increased risk of chronic kidney disease [Zhang 2019]. These studies analyzed the occurrence of AKI in patients with chronic renal impairment. In the field of cardiac surgery, the pathogenesis of acute renal impairment is not the same. The possible causes of AKI after

heart valve surgery are ischemia-reperfusion injury, hormone level disturbance caused by stress response, etc., rather than acute exacerbation of chronic disease of the kidney itself. Most patients have no chronic renal insufficiency, so these studies may not be universal and need to be verified separately. In the current study, we evaluated the independent predictive value of MLR, NLR, and PLR in patients undergoing heart valve surgery for postoperative AKI and found that higher preoperative MLR is associated with a significantly increased risk of postoperative AKI. First, the involvement of inflammatory response in the occurrence and development of heart valve disease widely has been recognized. Studies have shown that the detection of inflammatory factor-secreting mononuclear cell infiltration on the diseased valve tissue can lead to aggravation of valve disease. At the same time, it can detect a variety of inflammatory mediators such as interleukin, C-reactive protein, tumor necrosis factor, etc., which are also secreted by monocytes, and can chemotactic the expression of lymphocytes, further aggravating tissue damage. Monocytes also have been proven to play a role in lipid deposition and plaque formation in blood vessels. They are important participants in atherosclerosis. They develop into macrophages to phagocytose harmful substances, such as low-density lipoproteins. It secretes a variety of inflammatory mediators, and rheumatic heart valve disease also is a chronic inflammatory disease. Inflammation is involved in its occurrence and development. Patients with rheumatic heart disease often have different

Table 3.	Multivariate	logistic	regression	analysis	for	markers of AKI	

Variables	OR	95% CI	<i>P</i> -value
Multivariate analysis			
Hospitalization expenses (yuan)	1.000	1.000-1.000	0.38
LA	1.013	0.956-1.074	0.65
Creatinine (µmol/L)	1.018	1.000-1.035	0.04
MLR (≥0.47)	2.951	1.412-6.167	0.00
Monocyte (≥0.43×109/L)	2.567	1.128-5.864	0.03

AKI, acute kidney injury; OR, odds ratio; CI, confidence interval; MLR, monocyte to lymphocyte ratio

Table 4. Incidence of	postoperative com	plications in different	grades of MLR group

	MLR<0.47 ( <i>N</i> = 189)	MLR≥0.47 ( <i>N</i> = 142)	P-value
LCOS	7	19	0.00
RRT treatment	2	8	0.02
Arrhythmia*	41	42	0.10
Lung infection	22	20	0.51
Death in hospital	3	8	0.04

\*Severe arrhythmia manifested as atrial fibrillation, supraventricular tachycardia, multiple ventricular premature beats, ventricular tachycardia, ventricular fibrillation, etc. which lead to hemodynamic instability or cardiogenic shock; RRT, renal replacement therapy degrees of kidney damage, whether it is because of different degrees after valve replacement. Decreased renal blood perfusion caused by reduced heart function or systemic inflammatory response that affects the kidney. Various factors, such as ischemia-reperfusion injury caused by cardiopulmonary bypass, anesthesia, surgical stress and low temperature, can cause inflammation and damage the function of the kidney and multiple organs. This also is consistent with our results of elevated monocytes in valvular disease in this study [Kratofil 2017]. It can be seen in univariate and multivariate logistic regression analysis, monocyte counts are significantly correlated with the occurrence of postoperative AKI. The patients in the elevated monocyte group were grouped and studied, and it was confirmed that 29 people in the high monocyte group developed AKI after surgery, compared with only eight people in the low monocyte group. The difference statistically was significant. ROC curve sensitivity was 78.4%, specificity was 56.8%, and AUC was 0.717, P < 0.05, proving that it has a certain predictive value for postoperative renal function damage. As a new inflammatory marker, MLR is more stable and balanced than a single white blood cell subtype. This study also proved that the increase of MLR has statistical significance in the occurrence of postoperative AKI through univariate and multivariate regression analysis. The subjects were divided into two groups, according to the best cut-off value of MLR (0.43×109/L). Multivariate regression analysis showed that higher preoperative MLR ( $\geq 0.47$ ) independently predicted postoperative AKI (25 vs. 12, OR: 2.951, 95% CI: 1.412-6.167, P < 0.05). The difference was statistically significant. The sensitivity of ROC curve analysis was 89.2%, the specificity was 58.2%, and the AUC was 0.772. There is a certain predictive value. This indicates that the higher the MLR, the more severe the inflammatory response, the stronger the immunosuppressive effect, and the more likely it is to have an impact on renal function after surgery.

This study also analyzed the effects of MLR on postoperative complications and in-hospital mortality. It found that patients with higher preoperative MLR are more likely to have LCOS after surgery, more likely to use RRT to alleviate kidney damage and higher in-hospital mortality rate. The activation of the inflammatory response during valve disease will increase the severity of valve disease. The more severe the disease, the higher the difficulty and complexity of the operation, and the higher the risk of LCOS after surgery, which may damage other organs. This also is consistent with the analysis results of this research. Although there is no statistical difference in the incidence of postoperative pneumonia in this study, the data is not quantitative information obtained from laboratory indicators, but qualitative data for discharge diagnosis, so it may be different from the actual incidence. If the increase in MLR affects the function of multiple organs, it is not difficult to understand its impact on mortality. In this study, eight patients died in the high-value group and three patients died in the low-value group. The difference was statistically significant (P < 0.05), the mortality rate was about 3.6%, which is close to the mortality rate of normal heart valve surgery in our center, reflecting the huge impact of renal function damage on the prognosis of patients and also

suggesting this research has certain clinical application value.

In terms of baseline data, our study also found that the diameter of the left atrium is associated with postoperative kidney injury. Patients with a large left atrium are more likely to develop AKI after surgery. This may be related to myocardial fibrosis, myocardial remodeling, and atrial enlargement caused by valvular disease, which leads to a decrease in anterior cardiac output, weakened cardiac function, and an increase in the incidence of atrial fibrillation, resulting in a decrease in renal perfusion. At the same time, thrombus is easily formed in the enlarged left atrium. The shedding of thrombus leads to small blood vessel infarction, which also may affect kidney function. Intraoperative damage caused by radiofrequency ablation of atrial fibrillation, release of inflammatory mediators, longer operation time and extracorporeal circulation time also will affect renal function.

Our current study suggested that MLR, rather than NLR and PLR, was a useful marker for predicting postoperative AKI. This study has good clinical implication. The MLR is a low-cost biomarker of systemic inflammation, easily calculated from a complete blood cell count. Further studies are needed to elucidate the mechanism of MLR elevation and its association with postoperative AKI.

Several limitations should be mentioned. First, our research was a retrospective study from a single center, which might lead to a lack of powerful convincingness. Second, the inflammatory markers of MLR, NLR and PLR were not dynamically observed, which may affect the judgment of the association between them and AKI. Third, inflammatory markers, such as tumor necrosis factor- $\alpha$  and C reactive protein, were not included in the study. So large sample size, multicenter, perspective studies are needed to further confirm the initial findings of the present study. Currently, it cannot be recommended as a single diagnostic criterion for AKI but rather should be used in combination with detailed medical history, physical examination, and viable microbiological indicators. Finally, since we only considered MLR as a predictor of acute kidney injury after valve surgery, we did not recommend any treatment to improve MLR prior to cardiac surgery.

## CONCLUSION

In conclusion, this study shows that preoperative increase in MLR is associated with the risk of postoperative AKI. MLR can be used as a cost-effective marker of postoperative AKI in patients undergoing heart valve replacement surgery. It has a certain predictive value for early postoperative complications and in-hospital mortality, which can assist in predicting the prognosis of patients. At the same time, early identification of high-risk patients and early intervention treatment can reduce the occurrence of complications and improve the overall effect of heart valve surgery.

#### REFERENCES

Association AD. 2013. Diagnosis and classification of diabetes mellitus.

#### Diabetes Care.

Bellomo R, Auriemma S, Fabbri A, et al. 2008. The pathophysiology of cardiac surgery-associated acute kidney injury (CSA-AKI). Int J Artif Organs. 31:166-178.

Bonavia A, Singbartl K. 2018. A review of the role of immune cells in acute kidney injury. Pediatr Nephrol. 33:1629-1639.

Chen C, Zhao HY, Zhang YH. 2019. Correlation between neutrophilto-lymphocyte ratio and kidney dysfunction in undiagnosed hypertensive population from general health checkup. J Clin Hypertens (Greenwich).

Chen D, Xiao D, Guo J, Chahan B, Wang Z. 2019. Neutrophil-lymphocyte count ratio as a diagnostic marker for acute kidney injury: a systematic review and meta-analysis. Clin Exp Nephrol.

Fani F, Regolisti G, Delsante M, et al. 2018. Recent advances in the pathogenetic mechanisms of sepsis-associated acute kidney injury. J Nephrol. 31:351-359.

Gameiro J, Fonseca JA, Dias JM, et al. 2018. Neutrophil, lymphocyte and platelet ratio as a marker of postoperative acute kidney injury in major abdominal surgery. BMC Nephrol. 19:320.

Hobson CE, Yavas S, Segal MS, et al. 2009. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. Circulation. 119:2444-2453.

James PA, Oparil S, Carter BL, et al. 2014. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 311:507-520.

Joodi G, Maradey JA, Bogle B, et al. 2019. Coronary Artery Disease and Atherosclerotic Risk Factors in a Population-Based Study of Sudden Death. J Gen Intern Med.

Kellum JA NL, Aspelin P. 2012. Kidney disease: improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. Kidney international. Kratofil RM, Kubes P, Deniset JF. 2017. Monocyte Conversion During Inflammation and Injury. Arterioscler Thromb Vasc Biol. 37:35-42.

Nishimura RA, Otto CM, Bonow RO, et al. 2017. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 135:e1159-1159e1195.

Prowle JR, Calzavacca P, Licari E, et al. 2015. Combination of biomarkers for diagnosis of acute kidney injury after cardiopulmonary bypass. Ren Fail. 37:408-416.

Rabb H, Griffin MD, McKay DB, et al. 2016. Acute Dialysis Quality Initiative Consensus XIII Work Group. Inflammation in AKI: Current Understanding, Key Questions, and Knowledge Gaps. J Am Soc Nephrol. 27:371-379.

Romagnoli S, Ricci Z, Ronco C. 2018. Perioperative Acute Kidney Injury: Prevention, Early Recognition, and Supportive Measures. Nephron. 140:105-110.

Ronco C, Bellomo R, Kellum JA. 2019. Acute kidney injury. Lancet. 394:1949-1964.

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

Wu B, Chen J, Yang Y. 2019. Biomarkers of Acute Kidney Injury after Cardiac Surgery: A Narrative Review. Biomed Res Int. 7298635.

Zhang M, Wang K, Zheng H, Zhao X, Xie S, Liu C. 2019. Monocyte lymphocyte ratio predicts the new-onset of chronic kidney disease: A cohort study. Clin Chim Acta.

Zheng CF, Liu WY, Zeng FF, et al. 2017. Prognostic value of platelet-tolymphocyte ratios among critically ill patients with acute kidney injury. Crit Care. 21:238.