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Association between inflammatory biomarkers and postoperative acute kidney injury after cardiac surgery in patients with preoperative renal dysfunction: a retrospective pilot analysis

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Abstract

Background Acute kidney injury (AKI) represents a significant post-cardiac surgery complication, particularly prevalent among individuals with pre-existing renal dysfunction. Chronic kidney disease (CKD) is frequently accompanied by persistent, low-grade inflammation, which is known to exacerbate systemic stress responses during surgical procedures. This study hypothesizes that these inflammatory responses might influence the incidence and severity of postoperative acute kidney injury (AKI), potentially serving as a protective mechanism by preconditioning the kidney to stress.

Methods This retrospective study enrolled patients with preoperative renal dysfunction (eGFR between 15 and 60 ml/min/1.73 m^2) who underwent cardiac surgery between January 2020 and December 2022. Preoperative inflammatory biomarkers were evaluated. The primary outcome was the incidence of postoperative AKI, as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Multivariate regression models and sensitivity analyses were conducted to ascertain the relationship between inflammatory biomarkers and AKI. Restricted cubic spines (RCS) was conducted to explore nonlinear associations between inflammatory biomarkers and AKI.

Results AKI occurred in 53.4% (392/734) of patients, accompanied by significant mortality and length of hospital stay increases in cases of AKI ($P < 0.005$). After full adjustment of confounders, neutrophil percentage-to-albumin ratio (OR = 0.28), systemic inflammation response index (OR = 0.70), systemic immune inflammation index (OR = 0.69), neutrophil-to-lymphocyte ratio (OR = 0.70), monocyte/high-density lipoprotein cholesterol ratio (OR = 0.53), neutrophil/high-density lipoprotein cholesterol ratio (OR = 0.43) demonstrated an inverse association with AKI. Sensitivity analyses revealed that patients in the highest quartile of these biomarkers exhibited a significantly lower

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prevalence of AKI compared to those in the lowest quartile (p for trend < 0.05). The RCS analysis suggested an "Inverted U-shaped" association of both LnNPAR and LnSIRI with AKI.

Conclusions This study identified an inverse association between preoperative inflammatory biomarkers and postoperative AKI in patients with preoperative renal dysfunction. The findings implied that preoperative inflammation may play a protective role against postoperative AKI in this patient population undergoing cardiac surgery.

Keywords Cardiac surgery, Acute kidney injury, Risk factors, Inflammatory biomarker

Introduction

Cardiac surgery-associated acute kidney injury (AKI) is a serious and common complication following cardiac surgery [1]. AKI is associated with increased mortality and progression to end-stage renal disease, often necessitating dialysis and kidney replacement therapy [2]. With the rapid advancements in cardiac surgery technology, the number of procedures in developing countries like China has significantly increased, making it possible for more patients with renal insufficiency to undergo cardiac surgery. However, preoperative renal dysfunction remains a significant risk factor for adverse outcomes. The molecular mechanisms underlying AKI are not well understood, and no effective therapeutic strategies currently exist [3]. Therefore, efforts towards the prevention, early diagnosis, and treatment of AKI have garnered significant attention, particularly for patients with preoperative renal dysfunction.

Although numerous biomarkers, such as neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and tissue inhibitor of metalloproteinases-2× insulin-like growth factor-binding protein 7 (TIMP-2×IGFBP7), have been developed for early AKI screening [4–6], their diagnostic value in AKI superimposed on chronic kidney disease (CKD) has not been extensively validated. Moreover, their high costs limit their utility in economically underdeveloped regions. Recent studies have demonstrated that preoperative inflammatory biomarkers, which reflect the systemic inflammatory state, can predict outcomes in CKD and AKI [7–11]. These biomarkers, such as neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR), are easily obtained from routine blood tests and provide insights into the patient's baseline inflammatory status, which may influence their resilience to perioperative stress. CKD is associated with low-grade, persistent inflammation [12], and factors during cardiac surgery, such as cardiopulmonary bypass [13, 14] and blood transfusions [15, 16], exacerbate systemic inflammation and oxidative stress. Thus, understanding how preoperative inflammation in patients with preoperative renal dysfunction influences the risk of AKI during surgery is essential. Therefore, we focused on these systemic inflammatory biomarkers due to their established associations with inflammation and adverse outcomes in patients with cardiovascular and renal diseases. This study aims to evaluate the relationship between a series of preoperative inflammatory biomarkers and postoperative AKI in patients with preoperative renal dysfunction undergoing cardiac surgery.

Methods

Study population

We enrolled adult patients with preoperative renal dysfunction (eGFR between 15 and 60 ml/min/1.73 m^2) who underwent valve or coronary artery bypass surgery, or combined procedures, at our hospital between January 2020 and December 2022. Exclusion criteria included prior renal replacement therapy or transplant, preoperative AKI (KDIGO criteria [17]), incomplete medical records, death within 48 h of ICU admission, transferred from within the hospital, and emergent surgeries. The study was approved by the Zhongshan Hospital's Ethics Committee (Approval Number B2021–873R), and informed consent was obtained from all participants.

Study design

This retrospective study utilized clinical data extracted from electronic medical records, including demographics, comorbidities, laboratory results, surgical parameters, cardiopulmonary bypass (CPB) duration, postoperative medications, urine output, length of hospital stay, and mortality rates. Preoperative eGFR was calculated using the CKD-EPI equation [18] based on the most recent serum creatinine (SCr) measurement before surgery. Postoperative SCr was monitored daily in the ICU, with renal function tests conducted daily for the first three days post-ICU and every other day until discharge.

The primary outcome was the incidence of postoperative AKI, classified according to KDIGO guidelines. Participants were divided into two groups based on AKI development, allowing for a detailed investigation of various risk factors.

The secondary outcomes included the incidence of AKI stage 2–3, classified according to KDIGO guidelines and the length of hospital stay.

Definition of inflammatory biomarkers

Full blood counts were obtained from BD EDTA-K2 samples and analyzed using a Sysmex XN9000 electronic counter. Lymphocytes, neutrophils, and other blood cells were calculated based on their proportions from the total leukocyte count. We assessed inflammatory biomarkers, including the neutrophil percentage-to-albumin ratio (NPAR), systemic inflammation response index (SIRI), systemic immune inflammation index (SII), platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), monocyte/high-density lipoprotein cholesterol ratio (MHR), neutrophil/high-density lipoprotein cholesterol ratio (NHR), platelet/high-density lipoprotein cholesterol ratio (PHR), and lymphocyte/high-density lipoprotein cholesterol ratio (LHR).

NPAR = neutrophil percentage/serum albumin level (g/L), SIRI = neutrophil count × monocyte count/lymphocyte count, SII = platelet counts × neutrophil counts/lymphocyte counts, PLR = platelet counts/lymphocyte counts, MLR = monocyte counts/lymphocyte counts, NLR = neutrophil counts/lymphocyte counts, NHR = neutrophil counts/high-density lipoprotein cholesterol (HDL-C) (mmol/L), MHR = monocyte counts/HDL-C, LHR = lymphocyte counts/HDL-C, and PHR = platelet counts/HDL-C are the formulas for these inflammatory indicators. To measure HDL-C levels, Chemistry Analyzer Roche Cobas c702 and Roche modular P (Roche Diagnostics, Basel, Switzerland) were utilized.

Statistical analysis

Data analysis was conducted using R version 4.3.0. Normally distributed data were presented as mean ± standard deviation, non-normally distributed data as medians with interquartile ranges, and categorical variables as counts and percentages. We assessed normality and variance homogeneity using the Kolmogorov-Smirnov test. Differences in continuous data were determined using the Student t-test or nonparametric tests, while categorical variables were analyzed using Fisher's exact or chi-square tests.

We employed multivariable logistic regression models (Model 1 to Model 3) to examine associations between inflammatory biomarkers and AKI incidence, adjusting for confounders such as age, sex, surgery type, cardiopulmonary bypass duration, body mass index, history of hypertension, diabetes mellitus, recent myocardial infarction within one month, baseline eGFR, albumin, and hemoglobin. Considering that inflammatory biomarkers are skewed distribution and some of their values are relatively small, which might lead to less intuitive effect sizes, we performed a logarithmic transformation using the natural logarithm. We used restricted cubic splines (RCS) to address nonlinear relationships between potentially AKI-associated biomarkers, selecting models with the lowest Akaike information criterion value. When interpreting the results of an RCS analysis, the inflection point represented an inflection point or boundary between different patterns of association between the predictor variable and the outcome. In cases where the RCS analysis revealed a U-shaped, inverted U-shaped, or L-shaped curve, with a clearly identifiable inflection point, the data were divided into two distinct segments based on this inflection point. This segmented logistic regression allowed for a more nuanced understanding of the relationship between the predictor variable and the outcome in each segment, as it accounted for the distinct patterns of association in different parts of the curve. Predictive efficacy of inflammatory biomarkers was assessed using area under the curve (AUC) values and receiver operating characteristic (ROC) curves. Missing values for categorical variables were resolved using mode imputation, and median imputation was applied to continuous variables. Statistical significance was determined with a two-tailed p-value < 0.05.

Results

Basic characteristics

We enrolled 734 patients (Fig. 1) with preoperative eGFR between 15 and 60 ml/min/1.73 m^2; 53.40% (n = 392) developed AKI post-surgery. AKI stage 1: 258 patients (35.1%), stage 2: 81 patients (11%), stage 3: 53 patients (7.2%), 33 patients (4.5%) underwent RRT, and 48 patients (6.5%) died. Patients with AKI had higher mortality rates (9.44 vs. 3.22%, p < 0.001), longer ICU stays [64.00 (23.00–115.00) vs. 30.00 (21.00–69.00) hours, p < 0.001], and longer hospital stays [15 (12–22) vs. 15 (11–19) days, p = 0.004]. The AKI group was older, predominantly male, with higher incidences of hypertension. Laboratory evaluations indicated more severe renal dysfunction and lower preoperative hemoglobin and white blood cell in AKI patients. Combined surgeries and longer CPB durations were more common in the AKI group (Table 1).

Associations between inflammatory biomarkers and AKI

Our study revealed a negative association between NPAR, SIRI, SII, NLR, MHR, and NHR with AKI in the full adjusted Model 3 (LnNPAR: OR = 0.28; 95% CI: 0.09, 0.85; LnSIRI: OR = 0.70; 95% CI: 0.53, 0.91; LnSII: OR = 0.69; 95% CI: 0.51, 0.93; LnNLR: OR = 0.70; 95% CI: 0.49, 0.98; LnMHR: OR = 0.53; 95% CI: 0.36, 0.78; LnNHR: OR = 0.43; 95% CI: 0.25, 0.71). Patients in the highest quartile of these biomarkers had significantly lower AKI prevalence compared to the lowest quartile (p for trend < 0.05) (Table 2).

The RCS analysis, adjusting for the effects of age, preoperative eGFR, sex, surgical type, CPB duration,

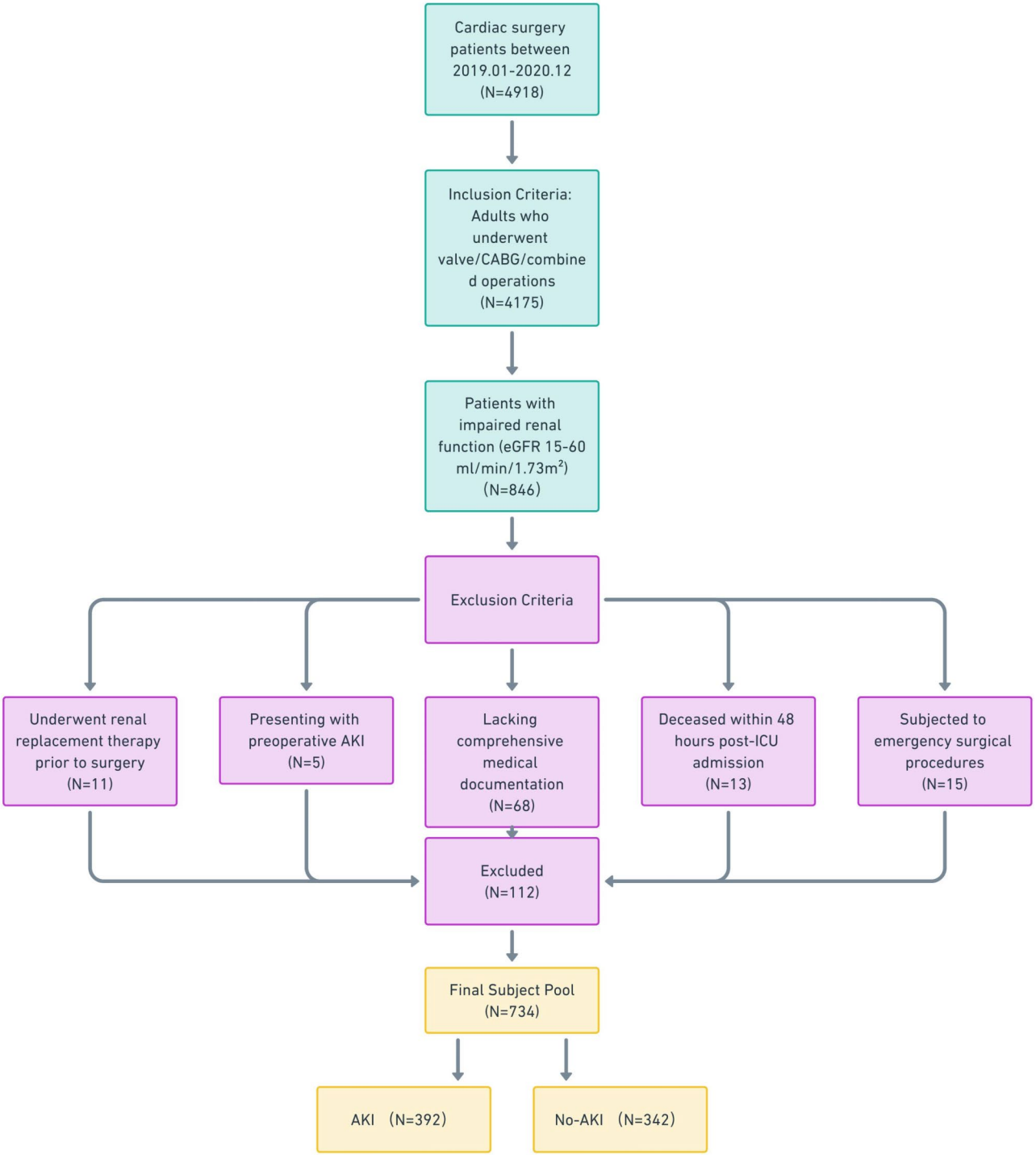

Fig. 1 Flowchart of the study design

body mass index (BMI), hypertension, diabetes mellitus, preoperative serum albumin, and preoperative hemoglobin suggested an "Inverted U-shaped" association of LnNPAR and LnSIRI with AKI. The inflection point of the RCS curve was identified at LnNPAR = 0.32 and LnSIRI=-0.22, representing an inflection point in their relationship between the LnNPAR (Fig. 2A) and LnSIRI (Fig. 2B) with the AKI. Using the inflection point, the data were stratified into two groups for each biomarker: (LnNPAR < 0.325 and LnNPAR ≥ 0.325) and (LnSIRI < -0.21 and LnSIRI ≥ -0.21). Segmented regression was then performed on each group separately, with the results presented in Supplementary Table S1. Over the respective inflection point, negative association was

Table 1 Perioperative characteristics of the study population

Characteristics	Total ($n=734$)	No-AKI ($n=342$)	AKI ($n=392$)	*p* value
Demographic data				
Male (%)	403 (54.90)	170 (49.71)	233 (59.44)	0.008
Age (years)	64.42 ± 9.95	63.63 ± 10.19	65.11 ± 9.70	0.044
BMI (kg/m^2)	23.27 ± 3.46	23.04 ± 3.33	23.48 ± 3.57	0.131
Pre-operative context				
Hypertension (%)	370 (50.41)	151 (44.15)	219 (55.87)	0.002
DM (%)	130 (17.71)	57 (16.67)	73 (18.62)	0.489
MI within one month (%)	26 (3.54)	15 (4.39)	11 (2.81)	0.248
Baseline laboratory indices				
Hemoglobin (g/L)	128.07 ± 17.58	129.70 ± 17.07	126.65 ± 17.92	0.019
Platelets (10^9/L)	186.07 ± 60.18	187.50 ± 58.50	184.82 ± 61.66	0.547
White blood cell (10^9/L)	7.19 ± 3.14	7.63 ± 3.58	6.82 ± 2.64	< 0.001
Neutrophil (%)	63.04 ± 11.91	64.43 ± 13.21	61.84 ± 10.51	0.004
Lymphocyte (%)	28.02 ± 9.85	27.75 ± 10.28	28.25 ± 9.47	0.495
Monocyte (%)	7.11 ± 2.36	7.18 ± 2.50	7.05 ± 2.22	0.472
RDW (%)	13.88 ± 1.68	13.93 ± 1.99	13.83 ± 1.36	0.436
Fasting blood glucose (mmol/L)	5.69 ± 2.06	5.78 ± 2.18	5.61 ± 1.96	0.291
Total cholesterol (mmol/L)	4.20 ± 1.06	4.15 ± 1.12	4.25 ± 1.01	0.285
Total triglycerides (mmol/L)	1.68 ± 1.36	1.59 ± 1.05	1.75 ± 1.56	0.170
LDL-C (mmol/L)	2.40 ± 0.88	2.37 ± 0.88	2.43 ± 0.89	0.420
HDL-C (mmol/L)	1.09 ± 0.35	1.08 ± 0.39	1.10 ± 0.32	0.670
Albumin (g/L)	39.35 ± 3.48	39.50 ± 3.38	39.21 ± 3.56	0.259
BUN (mmol/L)	9.83 ± 4.66	9.67 ± 5.16	9.98 ± 4.18	0.368
Serum creatinine (μmol/L)	127.20 ± 36.74	123.73 ± 36.01	130.23 ± 37.14	0.017
eGFR (ml/min/1.73m^2)	49.13 ± 9.45	50.01 ± 9.36	48.36 ± 9.48	0.018
Uric acid (μmol/L)	489.02 ± 221.65	463.34 ± 152.92	511.48 ± 265.87	0.003
NPAR (× 10^9/L/g)	1.62 ± 0.36	1.65 ± 0.38	1.59 ± 0.33	0.047
SIRI (10^9/L)	1.69 ± 2.61	2.00 ± 3.30	1.42 ± 1.76	0.004
SII (10^9/L)	589 ± 809	624 ± 845	559 ± 775	0.279
MHR (10^9/L/mmol/L)	0.52 ± 0.39	0.58 ± 0.50	0.47 ± 0.27	0.003
NHR (10^9/L/mmol/L)	5.02 ± 4.74	5.86 ± 6.33	4.36 ± 2.81	< 0.001
LHR (10^9/L/mmol/L)	1.93 ± 1.10	2.02 ± 1.17	1.85 ± 1.03	0.070
PHR (10^9/L/mmol/L)	188 ± 86	192 ± 88	184 ± 84	0.293
PLR	0.13 ± 0.13	0.13 ± 0.10	0.13 ± 0.16	0.837
NLR	3.03 ± 3.41	3.20 ± 3.77	2.89 ± 3.05	0.214
MLR	0.31 ± 0.22	0.32 ± 0.25	0.29 ± 0.20	0.120
Surgery				
Sole Valve (%)	418 (56.95)	200 (58.48)	218 (55.61)	0.052
Sole CABG (%)	260 (35.42)	124 (36.26)	136 (34.69)	0.978
Valve & CABG (%)	56 (7.63)	18 (5.26)	38 (9.69)	0.017
CPB duration (mins)	106.81 ± 79.17	96.75 ± 35.04	115.35 ± 102.05	0.011
Prognosis				
In-hospital mortality (%)	48 (6.54)	11 (3.22)	37 (9.44)	< 0.001
Length of ICU stay (hours)	45.00 (22.00, 90.75)	30.00 (21.00, 69.00)	64.00 (23.00, 115.00)	< 0.001
Length of hospital stay (days)	15.00 (12.00, 20.00)	15.00 (11.00, 19.00)	15.00 (12.00, 22.00)	0.004
Hospitalization cost (CNY)	88300.00 (67672.50, 119192.50)	82759.00 (62063.75, 109524.75)	94470.00 (70752.00, 123327.00)	< 0.001

AKI: Acute kidney injury; BMI: Body Mass Index; BUN: Blood Urea Nitrogen; CABG: Coronary Artery Bypass Grafting; CPB: Cardiopulmonary Bypass; DM: Diabetes Mellitus; eGFR: Estimated Glomerular Filtration Rate; HDL-C: High Density Lipoprotein Cholesterol; ICU: Intensive Care Unit; LDL-C: Low Density Lipoprotein Cholesterol; LHR: Lymphocyte to High-Density Lipoprotein Cholesterol Ratio; MI: Myocardial Infarction; MLR: Monocyte to Lymphocyte Ratio; MHR: Monocyte to High-Density Lipoprotein Cholesterol Ratio; NHR: Neutrophil to High-Density Lipoprotein Cholesterol Ratio; NLR: Neutrophil to Lymphocyte Ratio; NPAR: Neutrophil percentage-to-Albumin Ratio; PHR: Platelet to High-Density Lipoprotein Cholesterol Ratio; PLR: Platelet to Lymphocyte Ratio; RDW: Red Blood Cell Distribution Width; SII: Systemic Immune-Inflammation Index; SIRI: Systemic Inflammation Response Index

The values are expressed as the median (IQR) and mean ± SD or number (%)

P- values are the results of unpaired t-test or Mann–Whitney U test for continuous variables, and $\chi 2$ test or Fisher's exact test for categorical variables

Table 2 Association between inflammatory biomarkers and AKI (logistic regression)

Characteristic	Model 1			Model 2			Model 3		
	OR[1]	95% CI[1]	*p*-value	OR[1]	95% CI[1]	*p*-value	OR[1]	95% CI[1]	*p*-value
LnNPAR (continuous)	0.49	0.22, 1.07	0.075	0.47	0.21, 1.03	0.061	0.28	0.09, 0.85	0.025
NPAR									
Q1	—	—		—	—		—	—	
Q2	0.97	0.60, 1.55	0.883	0.95	0.59, 1.53	0.848	1.02	0.56, 1.85	0.953
Q3	1.06	0.65, 1.71	0.827	1.04	0.64, 1.70	0.861	0.77	0.42, 1.42	0.407
Q4	0.61	0.37, 0.98	0.043	0.59	0.36, 0.96	0.034	0.46	0.23, 0.91	0.026
p for trend			0.033			0.051			0.019
LnSIRI (continuous)	0.72	0.58, 0.88	0.002	0.71	0.57, 0.87	0.001	0.70	0.53, 0.91	0.008
SIRI									
Q1	—	—		—	—		—	—	
Q2	0.88	0.55, 1.42	0.604	0.82	0.50, 1.33	0.416	0.90	0.49, 1.65	0.740
Q3	1.02	0.63, 1.65	0.931	1.01	0.62, 1.63	0.973	1.16	0.64, 2.12	0.620
Q4	0.47	0.28, 0.78	0.004	0.45	0.27, 0.75	0.002	0.44	0.22, 0.83	0.013
p for trend			0.002			0.013			0.007
LnSII (continuous)	0.76	0.60, 0.96	0.025	0.74	0.58, 0.94	0.016	0.69	0.51, 0.93	0.014
SII									
Q1	—	—		—	—		—	—	
Q2	0.81	0.50, 1.31	0.401	0.81	0.50, 1.31	0.396	0.84	0.47, 1.51	0.566
Q3	0.94	0.58, 1.53	0.817	0.94	0.58, 1.52	0.799	0.98	0.54, 1.76	0.945
Q4	0.59	0.36, 0.96	0.034	0.57	0.35, 0.93	0.026	0.50	0.27, 0.93	0.029
p for trend			0.030			0.053			0.032
LnPLR (continuous)	0.79	0.55, 1.11	0.177	0.76	0.53, 1.08	0.133	0.69	0.45, 1.06	0.089
PLR									
Q1	—	—		—	—		—	—	
Q2	0.67	0.41, 1.08	0.098	0.68	0.42, 1.09	0.113	0.76	0.43, 1.34	0.339
Q3	0.81	0.50, 1.31	0.386	0.82	0.50, 1.33	0.419	0.82	0.45, 1.48	0.513
Q4	0.68	0.42, 1.10	0.119	0.65	0.40, 1.06	0.085	0.60	0.33, 1.09	0.098
LnMLR (continuous)	0.76	0.55, 1.04	0.090	0.76	0.55, 1.04	0.091	0.82	0.55, 1.21	0.316
MLR									
Q1	—	—		—	—		—	—	
Q2	1.00	0.62, 1.60	0.996	0.98	0.61, 1.58	0.947	1.12	0.62, 2.05	0.703
Q3	1.05	0.64, 1.70	0.858	1.04	0.64, 1.70	0.866	1.20	0.65, 2.23	0.566
Q4	0.71	0.43, 1.16	0.174	0.71	0.43, 1.16	0.176	0.80	0.43, 1.49	0.483
LnNLR (continuous)	0.75	0.56, 0.99	0.042	0.73	0.55, 0.97	0.033	0.70	0.49, 0.98	0.041
NLR									
Q1	—	—		—	—		—	—	
Q2	0.84	0.52, 1.35	0.464	0.81	0.50, 1.31	0.399	0.81	0.50, 1.32	0.405
Q3	0.86	0.53, 1.40	0.542	0.86	0.52, 1.39	0.529	0.77	0.47, 1.27	0.315
Q4	0.62	0.38, 1.01	0.053	0.60	0.36, 0.98	0.040	0.52	0.31, 0.86	0.011
p for trend			0.056			0.045			0.011
LnMHR (continuous)	0.57	0.39, 0.81	0.002	0.55	0.38, 0.79	0.002	0.53	0.36, 0.78	0.001
MHR									
Q1	—	—		—	—		—	—	
Q2	0.94	0.54, 1.64	0.824	0.90	0.51, 1.57	0.702	0.89	0.50, 1.56	0.680
Q3	0.81	0.45, 1.45	0.474	0.77	0.42, 1.38	0.375	0.74	0.40, 1.34	0.314
Q4	0.58	0.33, 1.03	0.062	0.56	0.32, 1.00	0.052	0.53	0.29, 0.97	0.041
p for trend			0.044			0.039			0.031
LnNHR (continuous)	0.53	0.37, 0.75	< 0.001	0.50	0.34, 0.71	< 0.001	0.43	0.25, 0.71	0.001
NHR									
Q1	—	—		—	—		—	—	
Q2	0.66	0.37, 1.17	0.157	0.67	0.38, 1.19	0.172	0.63	0.30, 1.31	0.221
Q3	0.74	0.41, 1.33	0.309	0.68	0.37, 1.24	0.207	0.63	0.29, 1.37	0.252

Table 2 (continued)

Characteristic	Model 1			Model 2			Model 3		
	OR[1]	95% CI[1]	*p*-value	OR[1]	95% CI[1]	*p*-value	OR[1]	95% CI[1]	*p*-value
Q4	0.37	0.20, 0.67	0.001	0.34	0.18, 0.62	< 0.001	0.32	0.14, 0.73	0.007
p for trend			< 0.001			0.008			0.009
LnLHR (continuous)	0.69	0.47, 0.99	0.048	0.67	0.46, 0.97	0.036	0.71	0.43, 1.13	0.160
LHR									
Q1	—	—		—	—		—	—	
Q2	0.72	0.41, 1.26	0.253	0.69	0.39, 1.22	0.202	0.71	0.34, 1.50	0.375
Q3	0.53	0.30, 0.92	0.026	0.50	0.28, 0.89	0.018	0.62	0.29, 1.30	0.206
Q4	0.75	0.42, 1.32	0.318	0.70	0.39, 1.25	0.230	0.61	0.28, 1.29	0.195
LnPHR (continuous)	0.72	0.45, 1.14	0.160	0.67	0.42, 1.07	0.098	0.61	0.32, 1.14	0.121
PHR									
Q1	—	—		—	—		—	—	
Q2	0.82	0.46, 1.43	0.482	0.82	0.46, 1.44	0.485	1.07	0.51, 2.21	0.863
Q3	0.63	0.35, 1.11	0.113	0.58	0.32, 1.04	0.067	0.61	0.29, 1.31	0.203
Q4	0.66	0.37, 1.17	0.156	0.61	0.34, 1.10	0.102	0.56	0.26, 1.23	0.149

NPAR: Neutrophil percentage-to-Albumin Ratio; SIRI: Systemic Inflammation Response Index SII: Systemic Immune Inflammation Index; PLR: Platelet-to-Lymphocyte Ratio; NLR: Neutrophil-to-Lymphocyte Ratio; MLR: Monocyte-to-Lymphocyte Ratio; MHR: Monocyte-to-High Density Lipoprotein Cholesterol Ratio; NHR: Neutrophil-to-High Density Lipoprotein Cholesterol Ratio; LHR: Lymphocyte- to-High Density Lipoprotein Cholesterol Ratio; PHR: Platelet-to-High Density Lipoprotein Cholesterol Ratio

In sensitivity analysis, inflammatory indexes were converted from continuous variables to categorical variables (quartiles)

[1]OR = Odds Ratio, CI = Confidence Interval

Model 1: adjusted for age, sex, surgery type, and body mass index

Model 2: adjusted for age, sex, surgery type, body mass index, history of hypertension, and history of diabetes mellitus

Model 3: adjusted for age, sex, surgery type, cardiopulmonary bypass duration, body mass index, history of hypertension, history of diabetes mellitus, history of myocardial infarction within one month, baseline eGFR, albumin and hemoglobin

found between LnNPAR (OR = 0.82, 95%CI 0.69, 0.97) and LnSIRI (OR = 0.74, 95%CI 0.61, 0.89) with AKI. The relationships between other biomarkers with AKI were revealed linear (Fig. 2C-F).

ROC analysis

Our results demonstrated that the AUC values for the biomarkers predicting AKI ranged from 0.514 to 0.565 (Supplementary Table S2), indicating varying degrees of predictive power. Notably, NHR had the highest AUC value of 0.565 (95% CI: 0.516–0.614), suggesting it was the most reliable predictor among the biomarkers studied. This was followed by MHR with an AUC of 0.551 (95% CI: 0.502–0.600) and SIRI with an AUC of 0.548 (95% CI: 0.506–0.590). The differences in AUC values highlighted the varying degrees of association between these inflammatory markers and the risk of developing AKI postoperatively.

Associations Between Inflammatory Biomarkers and AKI Stage 2–3.

Our study revealed a negative association between SIRI, SII, and PLR with AKI stage 2–3 after full adjustment (Model 3) (LnSIRI: OR = 0.68; 95% CI: 0.49, 0.97; LnSII: OR = 0.63; 95% CI: 0.42, 0.93; LnPLR: OR = 0.55; 95% CI: 0.31, 0.97). In addition, while continuous variable NLR was not significantly associated with AKI stage 2–3, the highest quartile of NLR presented significantly lower AKI prevalence compared to the lowest quartile ($p = 0.048$). Patients in the highest quartile of the above biomarkers had significantly lower AKI prevalence compared to the lowest quartile (p for trend < 0.05) (Table 3).

Associations Between Inflammatory Biomarkers and Length of Hospital Stay.

Positive linear association were found between NPAR, SIRI, SII, MLR, NLR, MHR, and NHR with length of hospital stay (LnNPAR: β = 10.70; 95% CI: 5.44, 15.97; LnSIRI: β = 2.38; 95% CI: 1.15, 3.62; LnSII: β = 1.73; 95% CI: 0.32, 3.14; LnMLR: β = 2.55; 95% CI: 0.66, 4.44; LnNLR: β = 2.42; 95% CI: 0.76, 4.08; LnMHR: β = 3.58; 95% CI: 1.30, 5.86; LnNHR: β = 4.18; 95% CI: 1.82, 6.53). Apart from MLR, patients in the highest quartile of these biomarkers had significantly lower AKI prevalence compared to the lowest quartile (p for trend < 0.05) (Table 4).

Discussion

This pilot study is the first to focus exclusively on patients with preoperative renal insufficiency. The selection of biomarkers to investigate was based on their proven relevance in reflecting systemic inflammation and predicting adverse outcomes in cardiovascular and renal disease populations, making them practical and valuable for clinical assessments. We found that elevated preoperative inflammatory biomarkers (NPAR, SIRI, SII, NLR, MHR, and NHR) were associated with a reduced risk of postoperative AKI. Trending analysis indicating that higher levels of these biomarkers are linked to lower AKI

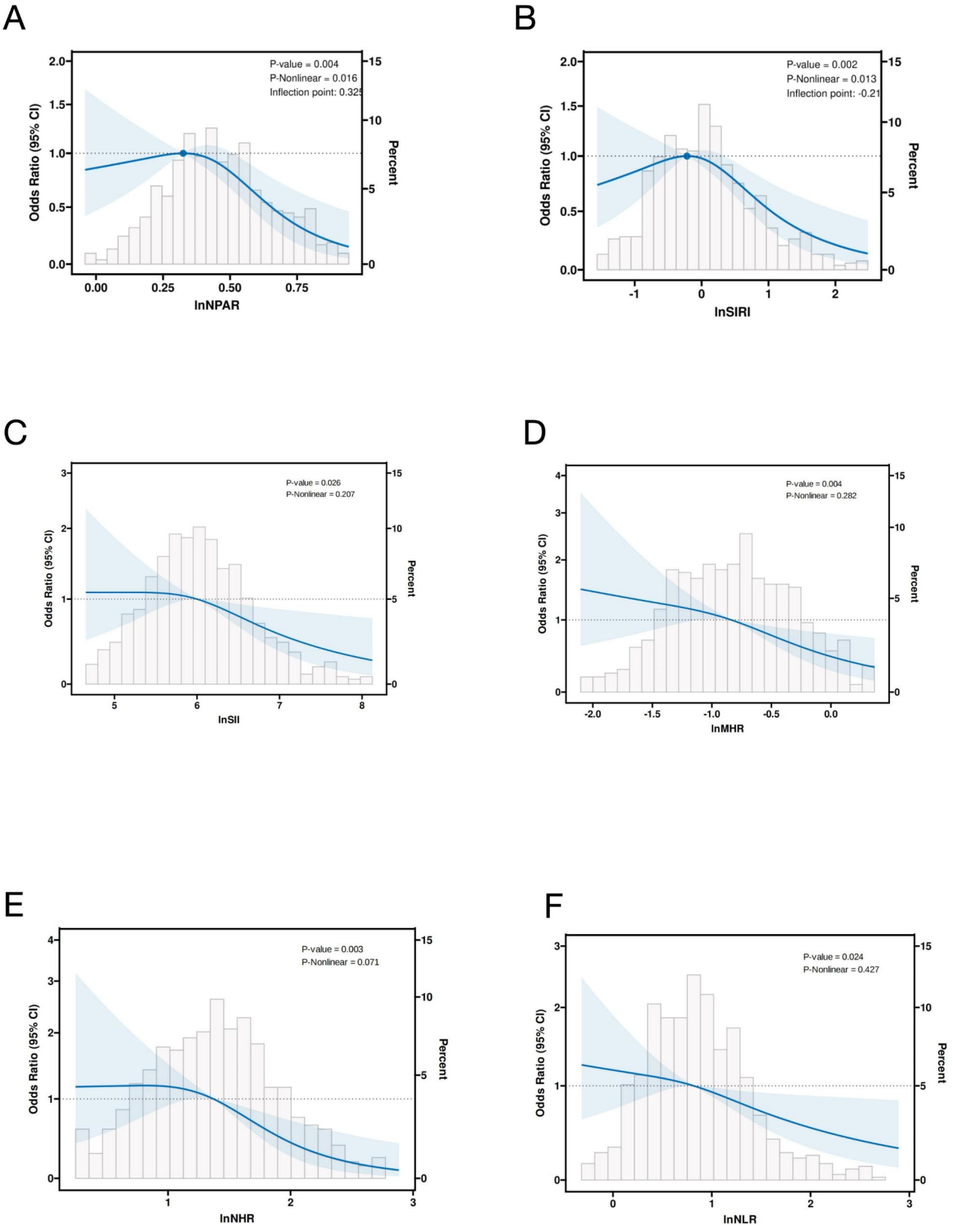

Fig. 2 Potential nonlinear relationship between the natural log-transformed inflammatory biomarkers and AKI. (**A**) Neutrophil percentage-to-Albumin Ratio (lnNPAR); (**B**) Systemic Inflammation Response Index (lnSIRI); (**C**) Systemic Immune-Inflammation Index (lnSII); (**D**) Monocyte-to-High-Density Lipoprotein Cholesterol Ratio (lnMHR); (**E**) Neutrophil-to-High-Density Lipoprotein Cholesterol Ratio (lnNHR); (**F**) Neutrophil-to-Lymphocyte Ratio (lnNLR)

Table 3 Association between inflammatory biomarkers and AKI stage 2–3 (logistic regression)

Characteristic	Model 1			Model 2			Model 3		
	OR[1]	95% CI[1]	*p*-value	OR[1]	95% CI[1]	*p*-value	OR[1]	95% CI[1]	*p*-value
LnNPAR (continuous)	0.49	0.17, 1.36	0.171	0.45	0.16, 1.26	0.128	0.30	0.07, 1.24	0.095
NPAR									
Q1	—	—		—	—		—	—	
Q2	0.93	0.51, 1.67	0.803	0.91	0.50, 1.64	0.746	0.85	0.41, 1.75	0.658
Q3	0.89	0.49, 1.62	0.710	0.86	0.47, 1.57	0.624	0.74	0.34, 1.55	0.425
Q4	0.65	0.34, 1.23	0.189	0.62	0.32, 1.16	0.140	0.60	0.26, 1.38	0.234
LnSIRI (continuous)	0.67	0.50, 0.89	0.006	0.65	0.49, 0.87	0.004	0.68	0.49, 0.97	0.031
SIRI									
Q1	—	—		—	—		—	—	
Q2	0.76	0.42, 1.37	0.360	0.74	0.40, 1.35	0.326	0.70	0.33, 1.49	0.354
Q3	1.00	0.56, 1.76	0.990	0.96	0.54, 1.71	0.894	1.21	0.60, 2.44	0.587
Q4	0.30	0.14, 0.64	0.002	0.29	0.14, 0.61	0.001	0.32	0.13, 0.78	0.012
p for trend			0.006			0.004			0.001
LnSII (continuous)	0.71	0.51, 0.98	0.037	0.70	0.50, 0.97	0.031	0.63	0.42, 0.93	0.020
SII									
Q1	—	—		—	—		—	—	
Q2	0.57	0.32, 1.04	0.067	0.57	0.31, 1.04	0.067	0.56	0.27, 1.16	0.117
Q3	0.66	0.37, 1.19	0.169	0.66	0.37, 1.19	0.166	0.62	0.31, 1.25	0.180
Q4	0.39	0.20, 0.75	0.005	0.38	0.20, 0.74	0.004	0.35	0.16, 0.79	0.011
p for trend			0.008			0.007			0.002
LnPLR (continuous)	0.68	0.42, 1.10	0.119	0.68	0.42, 1.11	0.123	0.55	0.31, 0.97	0.039
PLR									
Q1	—	—		—	—		—	—	
Q2	0.78	0.44, 1.40	0.412	0.82	0.46, 1.47	0.499	0.90	0.46, 1.75	0.750
Q3	0.65	0.35, 1.19	0.161	0.67	0.36, 1.25	0.209	0.55	0.26, 1.18	0.125
Q4	0.54	0.29, 1.01	0.053	0.53	0.28, 1.00	0.050	0.46	0.21, 0.98	0.044
p for trend			0.044			0.041			0.026
LnMLR (continuous)	0.68	0.44, 1.04	0.077	0.67	0.43, 1.03	0.069	0.80	0.49, 1.30	0.367
MLR									
Q1	—	—		—	—		—	—	
Q2	1.32	0.74, 2.34	0.343	1.30	0.73, 2.31	0.375	1.56	0.75, 3.25	0.238
Q3	0.72	0.38, 1.36	0.307	0.73	0.38, 1.39	0.332	0.94	0.43, 2.04	0.867
Q4	0.58	0.29, 1.13	0.107	0.57	0.29, 1.11	0.098	0.63	0.28, 1.42	0.266
LnNLR (continuous)	0.67	0.45, 0.99	0.043	0.65	0.44, 0.97	0.034	0.63	0.40, 1.01	0.055
NLR									
Q1	—	—		—	—		—	—	
Q2	0.70	0.39, 1.26	0.229	0.66	0.37, 1.20	0.175	0.82	0.40, 1.71	0.604
Q3	0.71	0.39, 1.28	0.253	0.68	0.37, 1.24	0.209	0.84	0.41, 1.76	0.650
Q4	0.40	0.21, 0.79	0.008	0.37	0.19, 0.74	0.004	0.44	0.20, 0.99	0.048
p for trend			0.009			0.006			0.002
LnMHR (continuous)	0.74	0.48, 1.14	0.172	0.70	0.45, 1.08	0.106	0.84	0.50, 1.40	0.495
MHR									
Q1	—	—		—	—		—	—	
Q2	0.72	0.36, 1.41	0.334	0.69	0.35, 1.37	0.288	0.99	0.43, 2.27	0.972
Q3	0.95	0.48, 1.87	0.888	0.90	0.46, 1.79	0.770	1.14	0.49, 2.63	0.766
Q4	0.71	0.35, 1.42	0.333	0.65	0.32, 1.31	0.226	0.97	0.40, 2.33	0.940
LnNHR (continuous)	0.70	0.45, 1.08	0.108	0.65	0.42, 1.01	0.055	0.58	0.32, 1.04	0.067
NHR									
Q1	—	—		—	—		—	—	
Q2	0.80	0.41, 1.56	0.514	0.79	0.41, 1.54	0.488	0.75	0.34, 1.67	0.480
Q3	0.92	0.47, 1.79	0.803	0.86	0.44, 1.69	0.658	0.58	0.25, 1.35	0.205
Q4	0.46	0.22, 0.97	0.042	0.40	0.19, 0.86	0.019	0.45	0.18, 1.14	0.091

Table 3 (continued)

Characteristic	Model 1			Model 2			Model 3		
	OR[1]	95% CI[1]	*p*-value	OR[1]	95% CI[1]	*p*-value	OR[1]	95% CI[1]	*p*-value
LnLHR (continuous)	0.96	0.62, 1.48	0.850	0.92	0.59, 1.42	0.698	0.96	0.58, 1.57	0.860
LHR									
Q1	—	—		—	—		—	—	
Q2	0.82	0.41, 1.63	0.566	0.78	0.39, 1.56	0.480	1.00	0.43, 2.33	0.999
Q3	0.93	0.47, 1.85	0.842	0.90	0.45, 1.79	0.762	1.08	0.47, 2.49	0.849
Q4	1.22	0.62, 2.39	0.562	1.13	0.57, 2.23	0.730	1.02	0.44, 2.37	0.956
LnPHR (continuous)	1.11	0.63, 1.96	0.720	1.05	0.59, 1.86	0.871	0.86	0.42, 1.76	0.676
PHR									
Q1	—	—		—	—		—	—	
Q2	1.29	0.66, 2.53	0.461	1.29	0.66, 2.54	0.461	1.59	0.71, 3.56	0.258
Q3	1.02	0.50, 2.10	0.951	1.04	0.51, 2.16	0.906	0.67	0.27, 1.66	0.387
Q4	1.15	0.57, 2.33	0.701	1.08	0.53, 2.21	0.833	0.87	0.35, 2.16	0.760

NPAR: Neutrophil-percentage to-Albumin ratio; SIRI: Systemic Inflammation Response Index SII: Systemic Immune Inflammation Index; PLR: Platelet-to-Lymphocyte Ratio; NLR: Neutrophil-to-Lymphocyte Ratio; MLR: Monocyte-to-Lymphocyte Ratio; MHR: Monocyte-to-High Density Lipoprotein Cholesterol Ratio; NHR: Neutrophil-to-High Density Lipoprotein Cholesterol Ratio; LHR: Lymphocyte- to-High Density Lipoprotein Cholesterol Ratio; PHR: Platelet-to-High Density Lipoprotein Cholesterol Ratio

In sensitivity analysis, inflammatory indexes were converted from continuous variables to categorical variables (quartiles)

[1]OR = Odds Ratio, CI = Confidence Interval

Model 1: adjusted for age, sex, surgery type, and body mass index

Model 2: adjusted for age, sex, surgery type, body mass index, history of hypertension, and history of diabetes mellitus

Model 3: adjusted for age, sex, surgery type, cardiopulmonary bypass duration, body mass index, history of hypertension, history of diabetes mellitus, baseline eGFR, albumin and hemoglobin

rates. Similar association was found between SIRI, SII, and PLR with AKI stage 2–3. On the other hand, positive linear association were found between NPAR, SIRI, SII, MLR, NLR, MHR, and NHR with length of hospital stay. Through RCS analysis, an "Inverted U-shaped" association of LnNPAR and LnSIRI with AKI was identified. Over their respective inflection point, negative association was found between LnNPAR and LnSIRI with AKI.

Low-grade, persistent inflammation in CKD patients can result from various factors, including uremia [19], oxidative stress [20], and comorbid conditions like diabetes and cardiovascular disease [21]. Inflammation in CKD is marked by elevated proinflammatory cytokines, leading to endothelial dysfunction [22, 23] and increased cardiovascular risk. Poor nutritional status and protein-energy malnutrition, common in CKD, are closely linked to inflammation [24]. For instance, low serum albumin levels reflect both poor nutrition and an inflammatory state. De Mutsert et al. found that low serum albumin in dialysis patients is associated with increased mortality due to inflammation rather than malnutrition [25], suggesting that targeting inflammation may improve outcomes more effectively than focusing solely on nutrition.

Previous studies have established a correlation between inflammatory biomarkers and AKI post-cardiac surgery. Wang et al. found that a higher preoperative monocyte-to-lymphocyte ratio significantly predicts AKI after cardiac valve surgery [26], suggesting MLR as a cost-effective AKI risk marker. Their study excluded patients with NYHA grades 3–4 and renal insufficiency, while our study focused on patients with preoperative renal dysfunction. A systematic review and meta-analysis confirmed that elevated neutrophil-lymphocyte ratios predict AKI post-cardiac surgery [27], reinforcing its clinical utility for risk stratification. Another study showed that higher neutrophil-to-lymphocyte ratios are associated with significant inflammatory responses and increased AKI risk in transcatheter aortic valve implantation patients [28]. Two studies with fewer than 400 patients identified that perioperative neutrophil-to-lymphocyte ratio changes predict acute renal failure post-coronary bypass with cardiopulmonary bypass [29, 30].

Regarding NPAR and AKI, a retrospective study with 5083 non-CKD patients found a higher neutrophil percentage-to-albumin ratio associated with increased contrast-associated AKI risk post-percutaneous coronary intervention [31]. NPAR was also an independent predictor of long-term mortality. Wang et al. found that higher NPAR levels significantly correlate with increased all-cause mortality in critically ill AKI patients [32].

Simultaneously, studies have shown that HDL possess anti-inflammatory and antioxidant properties [33]. Smith LE et al. conducted a randomized clinical trial with 391 subjects to analyze the relationship between HDL cholesterol concentration and AKI post-cardiac surgery [34]. They found that higher preoperative HDL levels are associated with a reduced incidence of postoperative AKI, a correlation that is enhanced with statin treatment. Additionally, Huang et al. conducted a retrospective study on 1505 patients undergoing cardiopulmonary bypass

Table 4 Association between inflammatory biomarkers and length of hospital stay (linear regression)

Characteristic	Model 1			Model 2			Model 3		
	β	95% CI[1]	*p*-value	β	95% CI[1]	*p*-value	β	95% CI[1]	*p*-value
LnNPAR (continuous)	13.20	8.72, 17.69	< 0.001	12.93	8.46, 17.41	< 0.001	10.70	5.44, 15.97	< 0.001
NPAR									
Q1	—	—		—	—		—	—	
Q2	-0.76	-3.44, 1.91	0.576	-0.83	-3.50, 1.83	0.540	-0.17	-2.95, 2.61	0.906
Q3	1.10	-1.63, 3.84	0.429	1.03	-1.70, 3.76	0.459	2.33	-0.53, 5.19	0.111
Q4	7.38	4.63, 10.12	< 0.001	7.20	4.46, 9.94	< 0.001	6.51	3.36, 9.66	< 0.001
p for trend			< 0.001			< 0.001			< 0.001
LnSIRI (continuous)	3.00	1.84, 4.16	< 0.001	2.96	1.80, 4.11	< 0.001	2.38	1.15, 3.62	< 0.001
SIRI									
Q1	—	—		—	—		—	—	
Q2	-0.24	-2.99, 2.52	0.867	-0.68	-3.45, 2.08	0.628	-0.09	-2.95, 2.76	0.949
Q3	3.46	0.70, 6.21	0.014	3.37	0.63, 6.11	0.016	3.10	0.28, 5.92	0.032
Q4	5.03	2.14, 7.92	< 0.001	4.80	1.92, 7.68	0.001	3.90	0.84, 6.96	0.013
p for trend			< 0.001			< 0.001			0.004
LnSII (continuous)	2.61	1.25, 3.97	< 0.001	2.50	1.14, 3.86	< 0.001	1.73	0.32, 3.14	0.017
SII									
Q1	—	—		—	—		—	—	
Q2	2.05	-0.74, 4.84	0.150	2.06	-0.72, 4.84	0.148	1.88	-0.91, 4.68	0.187
Q3	2.59	-0.20, 5.38	0.070	2.56	-0.23, 5.34	0.072	2.08	-0.72, 4.88	0.145
Q4	5.18	2.34, 8.01	< 0.001	5.04	2.21, 7.86	< 0.001	3.93	1.00, 6.85	0.009
p for trend			< 0.001			< 0.001			0.001
LnPLR (continuous)	0.99	-1.04, 3.02	0.339	0.85	-1.18, 2.87	0.411	0.46	-1.59, 2.51	0.661
PLR									
Q1	—	—		—	—		—	—	
Q2	1.39	-1.40, 4.18	0.329	1.55	-1.23, 4.33	0.275	0.68	-2.06, 3.42	0.626
Q3	0.62	-2.21, 3.45	0.667	0.77	-2.05, 3.60	0.591	0.91	-1.95, 3.76	0.534
Q4	0.43	-2.40, 3.26	0.766	0.19	-2.63, 3.01	0.896	-0.40	-3.25, 2.45	0.781
LnMLR (continuous)	2.64	0.79, 4.50	0.005	2.65	0.80, 4.50	0.005	2.55	0.66, 4.44	0.009
MLR									
Q1	—	—		—	—		—	—	
Q2	0.73	-2.03, 3.49	0.605	0.63	-2.13, 3.39	0.655	0.60	-2.30, 3.49	0.687
Q3	0.50	-2.35, 3.36	0.730	0.49	-2.35, 3.34	0.735	0.60	-2.37, 3.57	0.692
Q4	1.96	-0.92, 4.84	0.183	1.97	-0.90, 4.84	0.179	2.05	-0.94, 5.05	0.179
LnNLR (continuous)	2.99	1.38, 4.61	< 0.001	2.92	1.30, 4.53	< 0.001	2.42	0.76, 4.08	0.004
NLR									
Q1	—	—		—	—		—	—	
Q2	-0.88	-3.64, 1.88	0.533	-1.05	-3.81, 1.70	0.455	-0.26	-3.09, 2.56	0.855
Q3	3.45	0.63, 6.26	0.017	3.41	0.61, 6.22	0.017	2.93	0.03, 5.83	0.048
Q4	3.59	0.77, 6.41	0.013	3.40	0.59, 6.22	0.018	3.53	0.60, 6.46	0.019
p for trend			0.002			0.003			0.008
LnMHR (continuous)	4.37	2.23, 6.51	< 0.001	4.19	2.04, 6.35	< 0.001	3.58	1.30, 5.86	0.002
MHR									
Q1	—	—		—	—		—	—	
Q2	-0.81	-4.29, 2.67	0.649	-1.21	-4.70, 2.27	0.495	-2.25	-5.90, 1.39	0.226
Q3	3.14	-0.52, 6.80	0.094	2.74	-0.92, 6.40	0.143	0.14	-3.65, 3.92	0.943
Q4	6.29	2.76, 9.82	< 0.001	5.90	2.35, 9.46	0.001	6.32	2.43, 10.21	0.002
p for trend			< 0.001			< 0.001			0.001
LnNHR (continuous)	5.65	3.57, 7.72	< 0.001	5.36	3.26, 7.45	< 0.001	4.18	1.82, 6.53	< 0.001
NHR									
Q1	—	—		—	—		—	—	
Q2	-0.35	-3.89, 3.18	0.846	-0.29	-3.82, 3.24	0.871	-1.42	-5.07, 2.24	0.449
Q3	3.33	-0.31, 6.97	0.074	2.98	-0.68, 6.63	0.111	1.03	-2.79, 4.86	0.597

Table 4 (continued)

Characteristic	Model 1			Model 2			Model 3		
	β	95% CI[1]	*p*-value	β	95% CI[1]	*p*-value	β	95% CI[1]	*p*-value
Q4	7.12	3.49, 10.75	< 0.001	6.65	2.99, 10.32	< 0.001	5.91	1.84, 9.99	0.005
p for trend			< 0.001			< 0.001			0.005
LnLHR (continuous)	2.07	-0.20, 4.35	0.075	1.83	-0.45, 4.11	0.116	0.17	-2.19, 2.54	0.887
LHR									
Q1	—	—		—	—		—	—	
Q2	-0.26	-3.83, 3.31	0.885	-0.56	-4.12, 3.01	0.760	-1.84	-5.69, 2.00	0.348
Q3	2.08	-1.49, 5.65	0.254	1.78	-1.79, 5.34	0.329	-0.14	-3.95, 3.67	0.942
Q4	4.26	0.65, 7.86	0.021	3.71	0.08, 7.33	0.046	1.80	-2.09, 5.69	0.366
LnPHR (continuous)	3.20	0.25, 6.15	0.034	2.68	-0.29, 5.65	0.078	1.34	-1.91, 4.60	0.419
PHR									
Q1	—	—		—	—		—	—	
Q2	-0.73	-4.30, 2.84	0.690	-0.73	-4.29, 2.83	0.687	-0.92	-4.67, 2.83	0.631
Q3	2.44	-1.24, 6.11	0.194	2.32	-1.37, 6.01	0.219	0.26	-3.67, 4.19	0.897
Q4	3.69	0.03, 7.35	0.049	3.14	-0.54, 6.82	0.095	2.27	-1.82, 6.37	0.278

NPAR: Neutrophil percentage-to-Albumin ratio; SIRI: Systemic Inflammation Response Index SII: Systemic Immune Inflammation Index; PLR: Platelet-to-Lymphocyte Ratio; NLR: Neutrophil-to-Lymphocyte Ratio; MLR: Monocyte-to-Lymphocyte Ratio; MHR: Monocyte-to-High Density Lipoprotein Cholesterol Ratio; NHR: Neutrophil-to-High Density Lipoprotein Cholesterol Ratio; LHR: Lymphocyte- to-High Density Lipoprotein Cholesterol Ratio; PHR: Platelet-to-High Density Lipoprotein Cholesterol Ratio

In sensitivity analysis, inflammatory indexes were converted from continuous variables to categorical variables (quartiles)

[1] CI = Confidence Interval

Model 1: adjusted for age, sex, surgery type, and body mass index

Model 2: adjusted for age, sex, surgery type, body mass index, history of hypertension, and history of diabetes mellitus

Model 3: adjusted for age, sex, surgery type, cardiopulmonary bypass duration, body mass index, history of hypertension, history of diabetes mellitus, baseline eGFR, albumin and hemoglobin

surgery and found that an elevated MHR is a significant predictor of AKI [35]. Moreover, one recent study [36] demonstrated that recombinant CER-001 HDL infusion significantly increased survival rates, reduced systemic inflammation, and improved renal and hepatic function in a swine model of lipopolysaccharide-induced AKI and in a Phase 2a clinical trial involving septic patients. CER-001 treatment showed promising results by enhancing lipopolysaccharide scavenging, modulating the cytokine storm, reducing endothelial dysfunction, and preventing the progression to severe AKI in septic patients.

Our findings, however, indicated that higher preoperative NPAR, SIRI, SII, NLR, MHR, and NHR levels are inversely correlated with AKI risk, suggesting that preoperative inflammation may enhance renal resilience and protective mechanisms, reducing AKI susceptibility post-surgery. This phenomenon's mechanisms remain unclear but may involve adaptive responses triggered by low preoperative inflammation induced by pre-existing renal dysfunction. Prietl et al. investigated the immune response in hemodialysis (HD) patients with COVID-19 [37], discovering that chronic inflammation in these individuals might provide a protective effect against severe COVID-19 outcomes. In their study, HD patients showed stable levels of Th1 and Th17 cytokines and an increased presence of CD38 + CD8 + effector memory and TEMRA T cells, which remained less altered during COVID-19 compared to non-HD patients. This study suggests that the chronic inflammatory state in HD patients may modulate their immune response, potentially mitigating the severity of COVID-19. These findings indicate that chronic inflammation could have protective effects against severe acute inflammation in this vulnerable population, offering valuable insights into the role of chronic inflammation in preventing acute inflammatory responses.

Our study identified an inverted U-shaped nonlinear relationship between the LnNPAR and LnSIRI with the incidence of AKI. This finding suggested that moderate levels of these inflammatory markers may not have a clear impact on the risk of AKI whereas at higher levels of inflammation, a robust anti-inflammatory or adaptive immune response that mitigates the potential damage caused by inflammation. This phenomenon underscores the complexity of the inflammatory response in the context of AKI and highlights the need for a nuanced understanding of how different levels of inflammation affect renal outcomes.

Given that the severity of kidney dysfunction and the presence of diabetes could influence preoperative inflammation levels, we conducted relevant analyses (see Supplementary Table S3/S4). Our results showed that, except for LHR, all inflammatory markers were higher in the eGFR < 30 (ml/min/1.73m^2) group compared to the eGFR ≥ 30 (ml/min/1.73m^2) group. In the analysis based on diabetes status, we found that only PHR was

significantly higher in the diabetes group compared to the non-diabetes group, while the other markers showed no significant differences between the two groups. Our multivariable regression analysis adjusted for baseline eGFR and diabetes as covariates to account for these factors.

Limitations

The limitation of the present study is: (1). The study's retrospective nature means it relies on existing medical records, which may not capture all relevant data, leading to potential biases in data collection and analysis. (2). The study did not include measurements of cytokines such as interleukins and tumor necrosis factor, which could provide a more comprehensive picture of the inflammatory state and its impact on AKI. (3). Incomplete data on preoperative C-reactive protein (CRP) levels limited the ability to fully assess the inflammatory status of patients. (4). While the study suggests a negative correlation between preoperative inflammatory biomarkers and AKI, it does not establish a causal relationship due to its observational design. (5). The study was conducted at a single hospital, which may limit the generalizability of the findings to other populations or healthcare settings. (6). The study population may not be diverse enough, thus necessitating further research, particularly prospective studies with broader populations, to confirm and expand upon these results.

Conclusion

Our findings indicate that higher preoperative NPAR, SIRI, SII, NLR, MHR, and NHR levels are inversely correlated with AKI risk. Interestingly, our findings suggest that higher preoperative levels of certain inflammatory biomarkers are associated with a reduced risk of postoperative AKI. Moreover, an "inverted U-shaped" association was observed between both LnNPAR and LnSIRI and AKI, with a negative association appearing beyond their respective inflection points.

Abbreviations

AKI	acute kidney injury
AUC	area under the curve
CKD	chronic kidney disease
CPB	cardiopulmonary bypass
CRP	C-reactive protein
eGFR	estimated glomerular filtration rate
HDL-C	high-density lipoprotein-cholesterol
ICU	intensive care unit
KDIGO	Kidney Disease: Improving Global Outcomes
KIM-1	kidney injury molecule-1
LHR	lymphocyte-to-high-density lipoprotein cholesterol ratio
MHR	monocyte-to-high-density lipoprotein cholesterol ratio
MLR	monocyte-to-lymphocyte ratio
NGAL	neutrophil gelatinase-associated lipocalin
NHR	neutrophil-to-high-density lipoprotein cholesterol ratio
NLR	neutrophil-to-lymphocyte ratio
NPAR	neutrophil percentage-to-albumin ratio
PLR	platelet-to-lymphocyte ratio
RCS	restricted cubic splines
ROC	receiver operating characteristic
SCr	serum creatinine
SII	systemic immune inflammation index
SIRI	systemic inflammation response index
TIMP-2×IGFBP7	tissue inhibitor of metalloproteinases-2× insulin-like growth factor-binding protein 7

Supplementary Information

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Supplementary Material 1

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Author contributions

WJ, XD and JX designed and directed the study, WJ, DZ and XX participated in data collection and maintenance, DZ, YF and JX analyzed the data, WJ, YF and ZL interpreted the results and writing. JX, XX, XD and ZL participated in reviewing the manuscript, the maintenance of dataset and facilitating the acquisition of data. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the ethical board from Zhongshan Hospital, Fudan University (Approval Number B2021–873R). The requirement for informed consent was informed consent was obtained from all participants. The study was conducted in accordance with the Helsinki Declaration (WMA Declaration of Helsinki, 2013).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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