Original Article

Association of Preoperative Neutrophil to Lymphocyte Ratio with Early Postoperative Acute Kidney Injury Following Isolated Off-Pump Coronary Artery Bypass Grafting

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Abstract:

Objective: Acute kidney injury (AKI) is a frequent complication after off-pump coronary artery bypass grafting (OPCAB) that complicates recovery, increases treatment cost and mortality. Neutrophil to lymphocyte ratio (NLR) is a systemic inflammatory marker easily derived from complete blood count that has many prognostic potentials. The purpose of this study was to evaluate if there is an association of preoperative NLR with early postoperative AKI following isolated OPCAB.

Methods: This cross-sectional study was carried out in the Department of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD) on a total of 60 patients aged 31-70 years with no preoperative renal dysfunction undergoing isolated OPCAB between August 2021 and July 2022. Group A included 30 patients with preoperative NLR < 2.65 and Group B included 30 patients with preoperative NLR ≥2.65. Patients were monitored for development of early postoperative AKI according to serum creatinine criteria of Kidney Disease Improving Global Outcomes (KDIGO) 2012 guideline.

Results: Two patients from group A and twenty patients from group B developed early postoperative AKI ($p < 0.001$). Events of AKI were significantly higher in group B patients at all postoperative time points. Multivariate binary logistic regression analysis revealed preoperative NLR ≥2.65 as an independent predictor of early post OPCAB AKI ($p = 0.004$, OR = 13.746). In receiver operating curve (ROC) analysis area under curve (AUC) was 0.933 (95% CI 0.874-0.992, $p < 0.001$). It showed 90.91% sensitivity and 73.7% specificity at the pre-set cut off value of NLR at 2.65 where optimal predictability of post-OPCAB AKI occurred with 66.67% positive predictive value, 93.33% negative predictive value and 80% accuracy.

Conclusion: Preoperative NLR is significantly associated with early postoperative AKI following isolated OPCAB and therefore it should be incorporated in routine clinical practice for early prediction of AKI and implementing timely preventive strategies.

Keywords: *NLR,OPCAB,AKI*

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Introduction

Off-pump coronary artery bypass (OPCAB) surgery first became popular in the 1990s in an effort to lessen acute organ dysfunction caused by cardiopulmonary bypass (CPB). [1] OPCAB was anticipated to have a lower incidence

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of acute kidney injury (AKI) due to lack of CPB associated systemic inflammatory response, non-pulsatile flow, hemodilution, hemolysis, low output syndrome, and global hypoperfusion.[2] However, AKI still remains a serious and frequent morbidity after OPCAB with incidence ranging from 8% to 30%[3] and is an independent predictor of increased mortality irrespective of perioperative risk factors.[4] This may be attributed to renal ischemia brought on by poor hemodynamics, athero-embolism from side clamping of aorta and, intraoperative hemodynamic instability and global hypoperfusion due to displacement of the heart during distal anastomosis.[5]

Serum creatinine is an indirect and slow response marker of renal function that is influenced by numerous non-renal factors like age, race, sex, muscle mass, medication, nutrition and hydration status.[6] In the acute setting, more than 50% of kidney function is lost before serum creatinine even begins to rise.[7] Novel biomarkers for early prediction of AKI include neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), cystatin-C (CysC), liver type fatty acid-binding protein (L-FABP), tissue inhibitor of metalloproteinases-2 (TIMP-2), insulin growth factor binding protein-7 (IGFBP-7), interleukin-6 (IL-6), interleukin-18 (IL-18).[8] But high cost of assays and lack of adequate testing facilities impede their serial evaluation for routine assessment.

Atherosclerosis, the main cause of coronary artery disease (CAD), is an inflammatory disease in which immune mechanisms interact with metabolic risk factors.[9] Moreover, surgical revascularization triggers additional release of potent inflammatory mediators eliciting a systemic inflammatory response like syndrome in the postoperative period leading to major organ-related complications.[10]

Neutrophils are key effectors of the inflammatory cascade. Biopsies from patients and animal models with AKI revealed increased neutrophils in the peritubular capillary network of the outer medulla as early as 30 minutes after ischemia–reperfusion.[11] Neutrophils adhere to endothelial cells with the help of intercellular adhesion molecule-1 and P-selectin. Along with platelets and red blood cells they cause capillary plugging leading to vascular congestion.[12] Degranulation of

neutrophils, release of proteases, myeloperoxidase, cytokines and generation of reactive species can aggravate injury and damage endothelial and epithelial cells in the outer medulla.[13]

Neutrophils regulate the acute phase of inflammation within the first 24 hours but in later phases of AKI, infiltration of lymphocytes and macrophages predominates. Regulatory T cells are significant in renoprotection and renal regeneration processes through anti-inflammatory cytokine release and promoting tubular proliferation.[14] Higher risk of AKI has been related to neutrophilia due to associated pro-inflammatory function and lymphopenia & monocytopenia due to a lack of protective function.[15]

The neutrophil to lymphocyte ratio (NLR) is an inexpensive surrogate marker of systemic inflammatory response.[16] NLR has been demonstrated to effectively predict AKI and other adverse effects following CABG, though the cutoff value varied among different studies.[17-22] Preoperative NLR measured on the immediate day before surgery is an effective index reflecting inflammation and oxidative stress,[23] therefore, is expected to make an early identification of patients more susceptible to renal injury. The purpose of this study was to find the association of preoperative NLR with early postoperative AKI following isolated OPCAB in our population so that early preventive measures can be implemented to protect the renal function to the maximum extent.

Methods:

This comparative cross-sectional study was conducted on 60 patients who underwent isolated OPCAB by standard median sternotomy approach for ischemic heart disease at Department of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD) from 1st August 2020 to 31st July 2022. Approval for the study was obtained from the Ethical Review Committee of NICVD.

Patients with preoperative renal dysfunction (serum creatinine <1.5 mg/dl &/or eGFR < 60 mL/min/1.73m^2), severe left ventricular systolic dysfunction (LVEF < 30%), history of acute myocardial infarction, cerebrovascular accident or percutaneous coronary intervention in the last 30 days prior to operation, known acute infections, autoimmune disease, malignancy, hematological proliferative disease, systemic inflammatory disease, chronic obstructive pulmonary disease or peripheral vascular disease, low preoperative hemoglobin levels (<10 g/dl), ongoing steroid treatment or chemotherapy, prior history of undergoing cardiac surgery with or without CPB and patients who required emergency conversion to on-pump revascularization or re- exploration due to excessive bleeding or perioperative intra-aortic balloon pump were excluded from this study.

After obtaining informed written consent, meticulous history was taken, detailed clinical examination was performed and relevant investigation findings were recorded in a pre-

designed semi-structured questionnaire. Age, gender, body mass index (BMI), history of smoking, diabetes, hypertension, dyslipidemia, LVEF, coronary angiogram findings, preoperative and postoperative laboratory parameters (complete blood count, serum creatinine, eGFR, C-reactive protein), number of grafts given, duration of surgery, amount of blood products used, mechanical ventilation time, urine output, duration of inotrope support, length of stay in the intensive care unit and hospital and postoperative morbidity (renal dysfunction, arrythmia, wound infection, psychosis or respiratory compromise), mortality were recorded.

On day before surgery, blood sample was taken by venipuncture.Complete blood count was performed in EDTA tube using Beckman Coulter DxH 500 and serum creatinine was measured using Beckman coulter AU 480 at biochemistry laboratory of NICVD. eGFR was calculated using the 2005 MDRD formula. NLR was calculated by dividing number of neutrophils to number of lymphocytes.

Patients were divided into two groups. Group A included 30 patients with preoperative NLR< 2.65 and Group B had 30 patients with preoperative NLR ≥2.65. This cut-off value was set according to the findings of a similar retrospective study by Parlar & Şaşkin in 2018.[19]

All patients received a standard general anesthesia protocol for surgery through standard median sternotomy approach. Mean blood pressure was maintained above 60 mm Hg and blood glucose level was maintained between 120-180 mg/dL throughout the perioperative period.

Left internal mammary artery (LIMA) and great saphenous vein, radial artery or right internal mammary artery (RIMA) were harvested according to plan. Heparin, in a dose of 100-200 IU/kg of body weight, was administered to maintain an activated clotting time of >300 sec. LIMA was the preferred conduit for left anterior descending artery in all cases. The Octopus Evolution Tissue Stabilizer (Medtronic, Inc, Minneapolis, MN) was used in each patient to stabilize the target coronary artery. After opening the target coronary, the intra-coronary shunts were placed. All the distal anastomoses were performed with either 7-0 or 8-0 polypropylene suture. And proximal anastomoses with 6-0 polypropylene sutures with the assistance of a side-biting clamp in the ascending aorta. After completion of the coronary anastomoses, heparin was reversed with protamine at a dose of 1 mg/100 IU of heparin. All patients were given tablet aspirin in a dose of 75 mg per day commenced from postoperative day one onward.

Postoperatively patients were shifted to ICU and extubated when they became alert, hemodynamics were stable, proper ventilation was maintained and blood gas values were within safety levels. Antibiotic and analgesics were used following the standard protocol of the institution. Blood samples for serum creatinine were collected at 24 hours, 48hours, 72 hours and 7 days after surgery. Urine output was monitored until inotropic support was withdrawn. To obviate volume depletion and prerenal azotemia, fluid management was optimized.

The primary outcome variable was development of postoperative AKI according to serum creatinine criteria of KDIGO 2012 guideline where AKI was defined as increase in serum creatinine by ≥0.3 mg/dl (≥26.5 µmol/l) within 48 hours or increase in serum creatinine to e" 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days. [24]

Statistical analyses were performed using Statistical Packages for Social Sciences (SPSS) version

26. Continuous data were summarized by mean ± SD and categorical data as frequency distribution and percentage. To make comparison between groups, we performed Chi-square (χ^2) test or Fisher's exact test for qualitative data and independent sample t-test for quantitative data between preoperative NLR < 2.65 and e" 2.65 group. To assess performance of preoperative NLR as a biomarker for early detection of postoperative AKI, receiver operating characteristic (ROC) curve was generated and area under the curve (AUC) was calculated. To determine independent predictor of AKI, multivariate binary logistic regression analysis was performed among those variables which were found to be significantly different between the two groups on univariate analysis. For all analytic tests, the statistical significance threshold was set at 5% and a p value of d"0.05 was considered statistically significant. The summarized data were interpreted accordingly and then presented in the form of tables and figures.

Interest of the patients or their guardians were given the highest priority and confidentiality was maintained with safeguard of health and rights of the participants throughout the study.

Results:

There were no significant differences between the two groups in terms of demographics, risk factors, coronary angiogram findings, LVEF or baseline biochemical investigations (Table I).

Table-I

Comparison of preoperative demographic, clinical and biochemical characteristics

Patient's characteristics	Group A (n = 30)	Group B (n = 30)	p value
Age in years (mean ± SD)	53.10 ± 9.25	53.70 ± 7.48	0.783*
Male (%)	25 (83.33%)	24 (80%)	0.739**
Female (%)	5 (16.67%)	6 (20%)	
BMI in kg/m^2 (mean ± SD)	25.57 ± 3.64	23.95 ± 3.09	0.068*
Diabetes mellitus (%)	12 (40%)	16 (53.33%)	0.301**
Hypertension (%)	16 (53.33%)	19 (63.3	0.432**
Dyslipidemia (%)	15 (50%)	16 (53.33%)	0.796**
Smoking (%)	14 (46.67%)	19 (63.33%)	0.194**
Coronary angiogram findings			
SVD (%)	1 (3.33%)	0 (0%)	
DVD (%)	6 (20%)	8 (26.67%)	0.520**
TVD (%)	23 (76.67%)	22 (73.33%)	
Left main disease (%)	5 (16.67%)	9 (30%)	0.222**
LVEF (mean ± SD)	48.43 ± 8.15	50.00 ± 7.28	0.435*
Serum creatinine in mg/dL (mean ± SD)	1.05 ± 0.13	1.11 ± 0.13	0.097*
eGFR in mL/min/1.73m^2 (mean ± SD)	71.28 ± 9.56	67.04 ± 8.63	0.076*
CRP in mg/dL (mean ± SD)	3.03 ± 1.48	3.7 ± 1.89	0.132*

BMI = body mass index, SVD = single vessel disease, DVD = double vessel disease, TVD = triple vessel disease, LVEF = left ventricular ejection fraction, eGFR = estimated glomerular filtration rate, CRP = C reactive protein

*Independent sample t-test

**Chi-square test

Patients in group B had significantly higher neutrophil count ($p < 0.001$), lower lymphocyte count ($p < 0.001$), and higher NLR (4.85 ± 3.13 vs. 1.78 ± 0.48; $p < 0.001$) compared to group A patients (Table II). Other hematological indices had no significant difference between two groups.

There was no significant difference between the two groups in regards of total number of grafts ($p= 0.133$) or events of per-operative arrythmia ($p = 0.136$). However, patients in Group B had significantly increased duration of surgery ($p = 0.022$), increased amount of perioperative blood transfusion ($p < 0.001$) and decreased per-operative mean urine output ($p < 0.001$) compared to Group A patients (Table III).

Table IV summarizes comparison of postoperative attributes between the two groups. Patients in group B had significantly longer mechanical ventilation time ($p < 0.001$), longer duration of ICU stay ($p < 0.001$) and longer length of postoperative hospital stay ($p < 0.001$) compared to group A patients. No significant difference was found between two groups regarding postoperative blood loss ($p = 0.343$), need for ≥2 inotropes for > 24 hours ($p = 0.432$) or mean urine output measured in mL/kg/hour at 24 hours ($p = 0.125$), 48 hours ($p = 0.445$) and 72 hours ($p = 0.323$) after surgery. However, serum creatinine was significantly higher in group B patients compared to group A at 24 hours ($p < 0.001$), 48 hours ($p < 0.001$), 72 hours ($p < 0.001$) and 7 days ($p < 0.001$) after surgery.

Patients in group B also had significantly higher incidence of in hospital morbidity (80% vs. 20%; $p < 0.001$) in the form of renal dysfunction, arrythmia, wound infection, psychosis or respiratory compromise. There was no in hospital mortality during the study period.

Total 22 out of 60 patients developed early postoperative AKI, only 2 were from group A and 20 belonged to group B ($p < 0.001$). AKI incidence was significantly higher in group B patients at 24 hours ($p = 0.003$), 48 hours ($p < 0.001$), 72 hours ($p = 0.001$) and 7 days ($p = 0.001$) after surgery. Number of AKI cases were highest at 48 hours after surgery and declined afterwards in both groups. Only 9 cases from group B still had AKI at 7 days after surgery.(Table V).

Binary logistic regression analysis was done to assess predictors of early post OPCAB AKI. Potential predictors were preoperative NLR ≥2.65, duration of surgery and perioperative blood transfusion- which were found to be

significantly different between the two groups on univariate analysis. Multivariate logistic regression analysis identified only preoperative NLR ≥2.65 as an independent predictor of early postoperative AKI (p = 0.004) with highest odds ratio (OR = 13.746). Other variables showed insignificant association (p > 0.05) with OR < 1 (Table VI).

Area under the curve (AUC) value was calculated using the Receiver Operating Characteristic (ROC) curve to determine the quality of preoperative neutrophil to lymphocyte ratio as a biomarker to predict early post-OPCAB AKI (Figure 1). ROC curve analysis revealed an area under the curve (AUC) of 0.933, indicating preoperative NLR had an outstanding diagnostic accuracy for predicting early postoperative AKI. At our pre-set cutoff value of 2.65, preoperative NLR could optimally predict early post-OPCAB AKI with 90.91% sensitivity, 73.7% specificity, 66.67% positive predictive value, 93.33% negative predictive value and 80% accuracy (Table VII)

Table-II

Comparison of preoperative complete blood count

Hematological parameter	Group A (n = 30)Mean ± SD	Group B (n = 30)Mean ± SD	p value
Hemoglobin (g/dL)	12.78±1.45	12.38±1.48	0.298
ESR (mm in 1st hour)	14.93±11.15	20.40±11.11	0.062
Hematocrit (%)	38.19±4.13	36.70±3.72	0.150
Platelet count (/cmm)	250600±96008	238620±89853	0.620
Mean platelet volume (fL)	8.51±0.89	8.61±0.89	0.683
Total count of WBC (/cmm)	7935.0±2056.5	9021.7±2946.8	0.103
Neutrophils (/cmm)	4281.37±1141.38	6515.97±2583.50	<0.001
Lymphocytes (/cmm)	2557.13±931.26	1549.10±635.91	<0.001
Monocytes (/cmm)	576.90±230.32	536.95±162.88	0.441
Eosinophils (/cmm)	513.90±329.56	439.65±238.69	0.322
Basophils (/cmm)	2.5±1.69	1.67±1.13	0.782
Neutrophil to lymphocyte ratio	1.78±0.48	4.85±3.13	<0.001

ESR = Erythrocyte sedimentation rate, WBC = white blood cell Independent sample t-test

Table-III

Comparison of per-operative attributes

Per-operative attribute	Group A(n=30)	Group B(n=30)	p value
Duration of surgery in hours (mean ± SD)	4.61±0.61	5.15±1.09	0.022*
Number of grafts (%)			
One (%)	2 (6.67%)	0 (0%)	
Two (%)	6 (20%)	10 (33.33%)	0.133**
Three (%)	19 (63.33%)	16 (53.33%)	
Four (%)	1 (3.33%)	4 (13.33%)	
Five (%)	2 (6.67%)	0 (0%)	
Perioperative arrythmia (%)	5 (16.67%)	10 (33.33%)	0.136**
Perioperative blood transfusion in units(mean ± SD)	3.83 ± 0.70	5.03 ± 1.10	<0.001*
Per-operative urine output in mL/kg/hr(mean ± SD)	1.61 ± 0.29	1.06 ± 0.14	<0.001*

*Independent sample t-test
**Chi-square test

Table-IV

Comparison of postoperative attributes

Post-operative outcome	Group A (n =30)	Group B (n =30)	p value
Blood loss in mL (mean ± SD)	674.00 ± 381.47	813.33 ± 291.23	0.343*
Mechanical ventilation time in hours(mean ± SD)	6.55 ± 1.42	9.32 ± 3.82	< 0.001*
ICU stay in days (mean ± SD)	5.72 ± 0.61	9.60 ± 3.57	< 0.001*
Postoperative hospital stay in days(mean ± SD)	8.00 ± 1.91	11.43 ± 3.81	< 0.001*
Needed ≥2 inotropes for >24 hours	16 (53.33%)	19 (63.33%)	0.432**
Postoperative urine output in mL/kg/hr(mean ± SD)			
At 24 hours	1.25±0.28	1.17±0.24	0.125*
At 48 hours	1.40±0.24	1.39±0.20	0.445*
At 72 hours	1.25±0.29	1.28±0.22	0.323*
Postoperative serum creatinine in mg/dL(mean ± SD)			
24 hours after surgery	1.14 ± 0.14	1.43 ± 0.32	< 0.001*
48 hours after surgery	1.24 ± 0.14	1.61 ± 0.36	< 0.001*
72 hours after surgery	1.13 ± 0.15	1.40 ± 0.29	< 0.001*
7 days after surgery	1.08 ± 0.12	1.26 ± 0.24	< 0.001*
In hospital morbidity	5 (16.67%)	20 (66.67%)	< 0.001*
In hospital mortality	0	0	-

*Independent sample t-test
**Chi-square test

Table-V

Comparison of development of early postoperative AKI (Chi-square test)

Postoperative AKI	Group A (n = 30)f (%)	Group B (n = 30)f (%)	p value
AKI at 24 hours			
Stage 1	1 (3.33%)	11 (36.67%)	
Stage 2	0 (0%)	1 (3.33%)	
Stage 3	0 (0%)	0 (0%)	0.003
No AKI	29 (96.67%)	18 (60%)	
AKI at 48 hours			
Stage 1	2 (6.67%)	17 (56.67%)	
Stage 2	0 (0%)	3 (10%)	
Stage 3	0 (0%)	0 (0%)	<0.001
No AKI	28 (93.33%)	10 (33.33%)	
AKI at 72 hours			
Stage 1	1 (3.33%)	13 (43.33%)	
Stage 2	0 (0%)	1 (3.33%)	
Stage 3	0 (0%)	0 (0%)	0.001
No AKI	29 (96.67%)	16 (53.33%)	
AKI at 7 days			
Stage 1	0 (0%)	9 (30%)	
Stage 2	0 (0%)	0 (0%)	
Stage 3	0 (0%)	0 (0%)	0.001
No AKI	30 (100%)	21 (70%)	
Total AKI cases	2 (6.67%)	20 (66.67%)	<0.001

AKI = Acute kidney injury, f = frequency

Table-VI

Determinants of early postoperative AKI following OPCAB

Variables	β	SE	p value	OR	95% CI	
					Lower	Upper
Preoperative NLR ≥2.65	2.621	0.903	0.004	13.746	2.343	80.643
Duration of surgery	0.015	0.368	0.968	0.985	0.479	2.025
Perioperative blood transfusion	0.799	0.433	0.065	0.450	0.254	1.072

Multivariate binary logistic regression analysis. Data were expressed as Odds Ratio (OR).
β = coefficient for constant in the null model, SE= standard error around the coefficient for constant, CI= confidence interval, NLR= neutrophil to lymphocyte ratio

Table-VII

Analysis of performance of preoperative NLR at preset cutoff point to predict early postoperative AKI following OPCAB from ROC curve

Cut-off point	AUC	95% CI	Sensitivity	Specificity	p value	PPV	NPV	Accuracy
2.65	0.933	0.874-0.992	90.91%	73.7%	<0.001[s]	66.67%	93.33%	80%

AUC= area under the curve, PPV= positive predictive value, NPV= negative predictive value

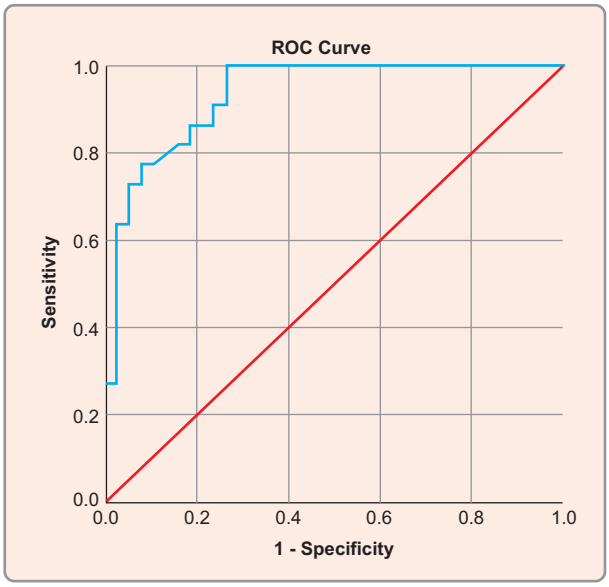

Figure 1: *Receiver operating characteristic (ROC) curve for preoperative NLR to predict early post-OPCAB AKI*

Discussion:

The major finding of this study was that elevated preoperative neutrophil to lymphocyte ratio (e"2.65) was associated with increased occurrence of early postoperative AKI. Group B patients, who were later found to develop increased incidence of postoperative AKI, had significant relative neutrophilia and lymphopenia compared to group A patients. This finding is in consistent with the U-shaped relationship between differential white blood cell count and risk of AKI & mortality in a prospective cohort of critically ill patients demonstrated by Seok Han et al.[15]

Patients in group B were found to have significantly reduced amount of per-operative urine output ($p < 0.001$). This could be an early manifestation of the increased incidence of postoperative AKI later found in this group. The increased preoperative NLR probably made these patients more susceptible to the additional insult by release of potent inflammatory mediators triggered by surgical revascularization resulting in increased incidence of postoperative AKI as suggested by Magoon & Makhija.[10]

In contrast to the findings of Parlar & Şaşkin [19], we found no significant difference of postoperative blood loss ($p = 0.343$) or duration of vasoactive inotropic support ($p = 0.432$) between the two groups. These findings further strengthen the fact that the association of preoperative NLR with postoperative AKI in our study was not confounded by postoperative anemia, hypovolemia or inotrope induced renal vasoconstriction.

Postoperative urine output measured at 24 hours ($p = 0.125$), 48 hours ($p = 0.045$) and 72 hours ($p= 0.323$) after surgery did not vary significantly between the two groups. Judicious use of diuretics, inotrope adjustment to maintain adequate cardiac output and thereby adequate renal perfusion as

well as meticulous monitoring of central venous pressure to optimize volume status in the ICU might have masked the reduced urine output expected in early stages of AKI.

In this study, serum creatinine showed gradual rise after surgery and peaked at 48 hours demonstrating the fact that it is an unreliable indicator during acute changes in kidney function rising late in the course of AKI.[24] Reno-protective measures were initiated in AKI patients by this time. As a result, serum creatinine showed a gradual decline in both groups at 72 hours and by 7 days after surgery almost neared baseline in group A patients.

As previously demonstrated by Parlar & Şaşkin [19] frequency of postoperative AKI was significantly higher at all time points in high preoperative NLR group. Over all, only 6.67% patients in group A developed postoperative AKI compared to 66.67% patients in group B ($p < 0.001$), indicating strong association between elevated preoperative NLR and early postoperative AKI.

The overall incidence of AKI following OPCAB in this study was 21.67% at 24 hours, 36.67% at 48 hours, 25% at 72 hours and 15% at 7 days. This correlates well with findings of previous studies that 5 to 30% of patients develop AKI after OPCAB with varying severity.[1,5,7]

Contrary to the findings of Dey et al.[18], we found that patients in group B had a significantly prolonged duration of surgery ($p = 0.022$). This prolonged operative period could be an indicator of longer time taken for distal anastomosis during which mechanical displacement of the heart was needed leading to a prolonged period of hemodynamic compromise which is a recognized risk factor for development of post OPCAB AKI.

We found patients in group B needed significantly increased amount of blood transfusion in the perioperative period. This finding is in agreement with the findings of Tewari, Pandye & Agarwal that intraoperative blood transfusion may increase the incidence of AKI in patients undergoing elective OPCAB.[25]

To determine if prolonged duration of surgery or increased amount of perioperative blood transfusion confounded the association between preoperative NLR and post OPCAB AKI, multivariate binary logistic regression analysis was performed. It revealed only preoperative NLR ≥ 2.65 as an independent determinant of post OPCAB AKI in our study ($p = 0.004$) with highest odds ratio (OR = 13.746).

Patients with high NLR were also found to require significantly prolonged duration of mechanical ventilation, length of ICU stay and length of postoperative hospital stay. This may be due to the fact that occurrence of in hospital morbidity, namely- renal dysfunction, arrythmia, psychosis, wound infection or respiratory complications were significantly higher in this group. These findings correlate well with a previous study by Dey et al. where increased preoperative NLR was found to be a predictor of adverse outcome after elective OPCAB.[18]

Our study revealed preoperative NLR has an outstanding potential to be used as an early predictor of post OPCAB AKI. AUC of the ROC curve for preoperative NLR was 0.933 ($p < 0.001$) with 90.91% sensitivity and 73.7% specificity at our preset cut off value of 2.65 where optimal predictability occurred with 66.67% positive predictive value, 93.33% negative predictive value and 80% accuracy. Parlar & Şaşkin found an AUC of 0.691 at a similar cut off value of 2.65 with 66.1% sensitivity and 64.7% specificity for preoperative NLR in predicting AKI after CABG.[19] The exclusion of on-pump cases may explain the remarkably improved diagnostic performance of preoperative NLR in our study. In another study, AUC of 0.981 with 98% sensitivity and 89.8% specificity at a cut off value of 4.625 for preoperative NLR was showed by Dey and colleagues in predicting poor outcome following elective OPCAB (Dey *et al.* 2020, p. 2403). But they defined new-onset renal failure in accordance with stage 3 of the AKIN criteria which might explain the increased cut off value in their study.

The present study revealed that patients with elevated preoperative NLR were more susceptible to develop post OPCAB AKI in spite of having no pre-existing renal impairment. The strength of this study was isolated inclusion of off-pump cases which obviated the consequences of hemodilution, cellular lysis, inflammatory and coagulation pathway activation associated with the use of an extracorporeal circuit in altering the baseline hematologic indices. Ischemia/reperfusion here was limited to the coronary artery territory being grafted. This allowed the opportunity of evaluating the exclusive effect of immediate preoperative day NLR on early postoperative AKI.

Preventive measures like identification of risk factors, avoiding nephrotoxic medication, dehydration and hyperglycemia, minimizing period of hemodynamic instability during distal grafting, maintenance of MAP and sinus rhythm, optimization of hemodynamics and intravascular volume with goal-directed protocols, judicious use of blood products, inotrope dose adjustment to maintain adequate renal perfusion, optimum diuresis etc. initiated early on in patients with elevated

baseline NLR may significantly reduce the incidence of post OPCAB AKI. As AKI prolongs the duration of ICU stay, complicates recovery, delays discharge and significantly increases the risk of chronic renal impairment and need for RRT in the long run, early prediction for timely intervention is of utmost need to reduce cost burden, morbidity and mortality. Since monitoring of AKI evolution with novel biomarkers is economically very challenging in our context, use of preoperative NLR for early prediction of postoperative AKI can be a very lucrative option in this case for its major asset of being cost-effective and easily available in daily clinical practice.

Conclusion:

This study revealed that elevated preoperative NLR is significantly associated with early postoperative AKI in patients undergoing isolated OPCAB. This result will encourage routine use of NLR as a biomarker for early prediction of post-OPCAB AKI after off-pump coronary artery bypass grafting and help to implement timely preventive measures.

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