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NLR and PLR as an indicator of outcomes following uneventful cardiac surgery

Vismay Bharath Shukla ¹, Ramesh H C ², Amulya Cherukumudi ^{1,*} and Varadaraju R ³

¹ Senior Resident, Department of Cardiothoracic and vascular surgery, Sri Jayadeva Institute of cardiovascular science and research, Bangalore, Karnataka, India.

² Associate Professor, Department of Cardiothoracic and vascular surgery, Sri Jayadeva Institute of cardiovascular science and research, Bangalore, Karnataka, India.

³ Professor and unit chief, Department of Cardiothoracic and vascular surgery, Sri Jayadeva Institute of cardiovascular science and research, Bangalore, Karnataka, India.

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Abstract

Background: Patients with coronary artery disease and valvular heart disease continue to be referred for cardiac surgery after medical management fails or in cases where it isn't feasible. These patients are susceptible to infection and inflammation due to previous MI, cardiopulmonary bypass and the stress associated with surgery itself. Most of these patients also have associated co-morbidities that further increases the risk of post-operative complication. Neutrophil/lymphocyte ratio (NLR) and Platelet/lymphocyte ratio (PLR) is a gaining popularity as a marker of inflammation. Hence we conducted this study to see if NLR and PLR can be used as indicators of outcomes following uneventful cardiac surgery.

Methods: A retrospective study was performed on patients undergoing off-pump CABG, on-pump CABG and valve surgeries. Demographic details was noted of all the patients. Postoperative outcomes such as ST-T changes, other arrhythmias, acute kidney/liver injury, wound infection or LRTI within 7 days of surgery was noted and documented. Surgery related factors- cross clamp time, bleeding, challenges in weaning off bypass and operative time were also recorded. Preoperative, day 1, and day 2 NLR and PLR was recorded.

Results: Two hundred and six patients in the study. Elevated Pre-op and post-op NLR and reduced PLR values was significantly associated with post-operative ST-T changes and LRTI, with a weak positive correlation between NLR and wound discharge. Additionally, we found that NLR and PLR showed a weak negative correlation with type II diabetes mellitus, pump time/ surgery time > 120 minutes and patients with history of recent MI. Higher preoperative NLR and reduced PLR was significantly associated with postoperative acute liver injury.

Conclusions: Higher preoperative and postoperative NLR and reduced PLR is associated with higher rates of complications post-cardiac surgery.

Keywords: Coronary artery bypass grafting; Neutrophil/lymphocyte ratio; Platelet/lymphocyte ratio; Valve replacement

1. Introduction

Coronary artery disease and valvular heart disease can and most often are managed medically or with interventional procedures such as balloon dilation or stenting. Once these fail, these patients referred for surgery, which remains the

* Corresponding author: Amulya Cherukumudi

gold standard care. Despite the improving expertise and techniques, there is still an associated mortality and morbidity due to the complexity of the surgery as well as the underlying patient factors as well.

It is observed that surgeries performed on cardiopulmonary bypass induces a state of SIRS, which further increases the risk of post-operative complications, and increases mortality and morbidity. While in some centers in India, off-pump coronary bypass grafting is the standard of care for CAD, most centers globally still prefer performing the same on-pump. Patients undergoing anaesthesia for cardiac surgery experience a systemic inflammatory response that is more indignant than in other surgeries due to the added stress of extracorporeal circulation [3,4]. This is because extracorporeal circulation requires the patient to have a higher level of blood pressure than normal during the procedure. In the medical literature, a number of haematological indices are mentioned as having varying degrees of predictive power depending on the clinical setting. The perioperative NLR and PLR, which can be used independently or as a pair, have been evaluated for their ability to predict postoperative morbidity and mortality as well as severe associated complications in patients undergoing cardiac surgery, with results that are sometimes favourable and other times unclear. These indices, to a certain extent, reflect the magnitude of the inflammatory response that takes place after the trauma of an operation [5,6].

Elevation in neutrophils with a reduction in lymphocytes is a hallmark of acute inflammatory changes due to T4H cells and IL6. NLR is gaining popularity in recent times to predict post-operative outcomes. However, there is little to no literature for use of NLR and PLR in post-cardiac surgery complications. (7,8)

This aim of this study was to find a cost-effective and easily available marker for predicting post-operative morbidity and mortality in cardiac surgery patients.

2. Material and methods

A prospective + retrospective study of all adult patients over 6 months period that underwent cardiac surgery for varying reasons for the first time. Data was collected from case records of patients operated between Feb 2022 to January 2023. Patients were excluded if they were under 18 years of age, of-pump procedures, infective endocarditis or if they succumbed to the surgery within 72 hours of the procedure.

Demographic details, brief clinical history, details of co-morbidities, baseline NLR and PLR, and postoperative NLR and PLR on day 1 and day 2 were collected. Postoperative CBC samples obtained on postoperative days 1 and 2 were used to record neutrophil and lymphocyte levels.

Any ST-T changes or arrhythmia was recorded, along with derangement in serial renal or liver function. This was all entered into a semi-structured proforma.

2.1. Statistical analysis

Descriptive analyses were provided using mean and standard deviation for continuous data, and absolute values and percentages for categorical data. A P value <0.05 was considered statistically significant.

3. Results

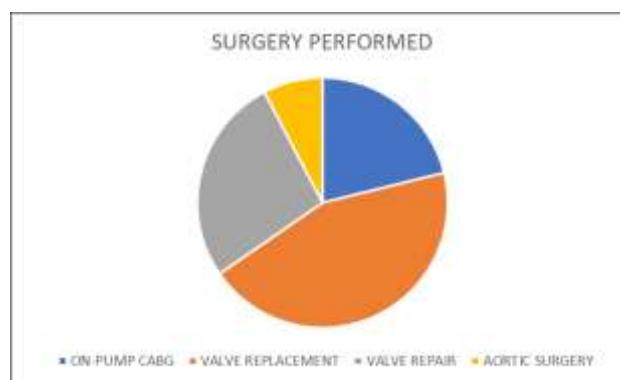


Figure 1 Surgeries performed in the study population

There were 264 cardiac procedures involving CABG or valve repair/replacement for primary valve pathology in our unit between February 2022 and January 2023 for whom full records were available. Of these, one hundred and sixty two patients were excluded from analysis as they previously undergone surgery without CPB or had a previous sternotomy.

Two hundred and six patients included in the study, and their data was analysed prospectively. For those patients that were operated, some pre-operatively laboratory values were collected retrospectively.

Mean age of the study participants was 62.34 +/- 18.4 years, and 62.4% were males. When we analysed the surgeries, valve replacement was the most common procedure.

The most common co-morbidity observed was type II diabetes mellitus followed by systemic hypertension.

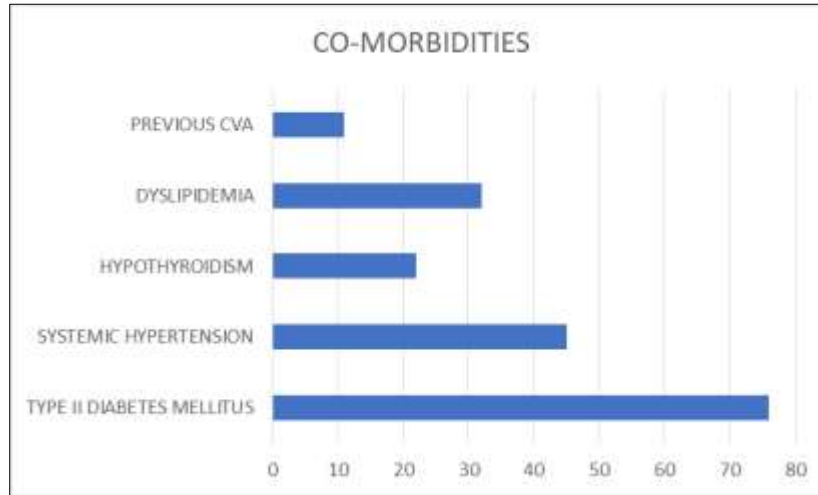


Figure 2 Associated co-morbidities in the study population

Mean CPB time was 114.56 +/- 27.54) and mean cross-clamp time was 94.67 minutes +/- 20.49.

Table 1 Changes in the NLR following surgery

	PRE-OP NLR	DAY 3 NLR	DAY 3 NLR	DAY 7 NLR
NORMAL	184 (160.22) [3.53]	143 (160.22) [1.85]	147 (160.22) [1.09]	168 (156.33) [0.28]
HIGH	22 (45.78) [12.35]	63 (45.78) [6.48]	59 (45.78) [3.82]	38 (44.67) [1.00]
Column Totals	206	206	206	206

In this study, when we analyzed the NLR values pre-operative and post-operatively, it was found to be elevated, and this using Pearson’s chi-square statistic is 30.3993. The p-value is < 0.00001, which is statistically significant.

Table 2 Changes in the PLR following surgery

	PRE-OP PLR	DAY 3 PLR	DAY 5 PLR	DAY 7 PLR
NORMAL	149 (160.22) [2.89]	156 (154.22) [1.66]	157 (156.47) [1.09]	164 (156.33) [0.34]
LOW	58 (54.78) [13.72]	50 (45.78) [5.78]	49 (45.78) [3.82]	42 (44.67) [1.44]
Column Totals	206	206	206	206

In this study, when we analyzed the NLR values pre-operative and post-operatively, it was found to be elevated, and this using Pearson’s chi-square statistic is 28.5623. The p-value is < 0.00001, which is statistically significant.

When we correlated NLR and PLR, we found a negative correlation with type II diabetes mellitus and hypertension.

However, when we correlated the type of surgery with the NLR, we didn't find any statistically significant difference. (p value 0.322)

Table 3 Correlation of the type of surgery with NLR

	PRE-OP	DAY 3 NLR	DAY 5 NLR	DAY 7 NLR
CABG	6 (3.87) [1.17]	10 (11.08) [0.10]	8 (10.37) [0.54]	8 (6.68) [0.26]
VALVE REPLACEMENT	10 (13.78) [1.04]	42 (39.46) [0.16]	40 (36.96) [0.25]	22 (23.80) [0.14]
VALVE REPAIR	4 (3.38) [0.11]	8 (9.69) [0.30]	9 (9.08) [0.00]	7 (5.85) [0.23]
AORTIC SURGERY	2 (0.97) [1.10]	3 (2.77) [0.02]	2 (2.59) [0.14]	1 (1.67) [0.27]
Column Totals	22	63	59	38

Similarly, when we correlated PLR with type of cardiac surgery, we found now difference. (p value 0.143)

3.1. Post-operative complications

Elevated Pre-op and post-op NLR and reduced PLR values was significantly associated with post-operative ST-T changes and LRTI, with a weak positive correlation between NLR and wound discharge. Additionally, we found that NLR and PLR showed a weak negative correlation with type II diabetes mellitus, pump time/ surgery time > 120 minutes and patients with history of recent MI. Higher preoperative NLR and reduced PLR was significantly associated with postoperative acute liver injury.

4. Discussion

Cardiac surgery is the gold standard treatment for many patients with coronary artery disease and valvular heart diseases. In this era of low mortality rates, surgeons are now striving to improve morbidity. It has been shown that increased inflammation from patient factors, choice of anaesthetic, degree of surgical trauma, degree of myocardial ischaemia, and duration of cardiopulmonary bypass can lead to complications, such as atrial fibrillation and acute kidney injury after cardiac surgery. Studies have shown that patients who develop POAF may have increased acute oxidative stress compared with matched patients who remain in sinus rhythm after cardiac surgery (13), suggesting an individual susceptibility to develop complications related to inflammation. The phenomenon of increased inflammation associated with cardiopulmonary bypass is well established. CPB activates contact systems of plasma proteins, intrinsic coagulation, extrinsic coagulation, complement, and fibrinolytic pathways, as well as activating platelets, neutrophils, monocytes, endothelial cells, and lymphocytes (14). Thrombin and other coagulation components and their products have proinflammatory effects. Thrombin also has direct chemotactic activity for neutrophils (15).

This study showed that neutrophil/lymphocyte ratio can be used to predict complications post cardiac surgery.

A 2010 study by Gibson *et al.* looked at 275 patients undergoing CABG in their institution over a 21-month period (7). The Gibson *et al.* study looked at preoperative NLR and day 2 NLR, as well as other leukocyte values and CRP. They found that preoperative NLR was not associated with POAF as a continuous variable, but that it was significantly associated with POAF as a dichotomous variable around a cut off of 2.63.

A study by Durukan *et al.* in 2014 assessed 523 patients over an 18-month period undergoing elective on-pump CABG in their institution. The Durukan *et al.* study also assessed preoperative NLR and day 2 NLR. 17.4% of patients developed POAF in their study, much lower than the number of patients in both the Gibson study, and the present study.

Inflammation plays a major role pathophysiology of LRTI, acute kidney injury and acute hepatic derangement. In keeping with the literature, age > 65 years, type II diabetes mellitus and longer CPB time were independently significantly associated with AKI post cardiac surgery.

A 2015 study by Kim *et al.* to assess the association between NLR and AKI post cardiac surgery with cardiopulmonary bypass included 590 patients where 28.1% developed AKI in the first 7 postoperative days (8). They also demonstrated that preoperative NLR did not predict postoperative AKI, similar to the findings of the current study. They found that immediate postoperative, and day 1 NLR were significant predictors of AKI. In the current study, the association

between day 1 NLR and AKI was not significant. However, the present study examined day 2 NLR and found a significant link between raised day 2 NLR and AKI.

In a study carried out by Gergios Taikos and colleagues (23), From among all of the parameters that were investigated, it was discovered that the NLR5 and NLR7, in addition to the PLR3, exhibited good discriminatory performance when it came to predicting 90-day mortality. Following this, a multivariate analysis was carried out, which revealed that NLR7 and the length of time spent in the intensive care unit were independent risk factors for death, even after taking into account age, gender, and MUST score. Other studies have also confirmed that the length of time spent in the intensive care unit is an independent risk factor. These studies found that postoperative morbidity and mortality were higher in patients who had spent a longer amount of time in the intensive care unit after cardiac surgery. In addition, respiratory events and extended periods of time spent intubated with a ventilator are the primary contributors to a longer length of stay in the hospital. According to the findings of our research, the majority of patients who passed away had been intubated for more than forty-eight hours while they were being treated in the intensive care unit. It is also important to note at this point that the preoperative MUST score, which is an indicator of patients' nutritional status, was not associated with increased mortality in the multivariate analysis model. This is because there was no difference found in the median MUST score between the patients who died and those who survived.

5. Conclusion

NLR is elevated and PLR is reduced in post-operative complications such as LRTI, ST-T changes and acute liver failure. It also has an association with type II diabetes mellitus and hypertension.

Hence, these can be used as predictors of poor outcomes in patients undergoing cardiac surgery,

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

This is Retrospective study.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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