[Turkish Journal of Medical Sciences](https://journals.tubitak.gov.tr/medical)

Volume 48 | Number 5 Article 21

1-1-2018

The effect of neutrophil-lymphocyte ratio on the postoperative course of coronary arterybypass graft surgery

ABDULLAH ÖZER

BARIŞ MARDİN

YİĞİT KILIÇ

GÜRSEL LEVENT OKTAR

ERKAN İRİZ

See next page for additional authors

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2018) 48: 1036-1040
© TÜBİTAK
doi:10.3906/sag-1804-94

The effect of neutrophil-lymphocyte ratio on the postoperative course of coronary artery bypass graft surgery

Abdullah ÖZER[1,*], Barış MARDİN[1], Yiğit KILIÇ[2], Levent OKTAR[1], Erkan İRİZ[1], Mustafa ARSLAN[3], Yusuf ÜNAL[3], Metin ALKAN[3]

[1]Department of Cardiovascular Surgery, Faculty of Medicine, Gazi University, Ankara, Turkey
[2]Pediatric Cardiovascular Surgery Clinic, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Training and Research Hospital, Haydarpaşa, İstanbul, Turkey
[3]Department of Anesthesiology and Reanimation, Faculty of Medicine, Gazi University, Ankara, Turkey

Received: 13.04.2018 • **Accepted/Published Online:** 21.09.2018 • **Final Version:** 31.10.2018

Background/aim: Recovery after coronary artery bypass graft surgery (CABG) can be complicated, leading to postoperative morbidity. The roles of hematologic and surgery-related parameters are important. The main purpose of this study is to determine the role of preoperative and postcardiopulmonary bypass neutrophil/lymphocyte ratio (NLR) on postoperative recovery.

Materials and methods: Sixty-two patients aged between 41 and 80 years, scheduled for elective CABG surgery with ASA I–II risk and without a history of preoperative blood transfusion, were included in the study. Three patients were excluded due to their need for additional surgical procedures other than CABG. The patients were divided into two groups that were formed *depending* on preoperative *NLR* cut-off values *below (Group 1, n = 37)* and *above 4 (Group 2, n = 22)*. Postoperative data such as length of stay in the hospital and in the intensive care unit (ICU), chest tube drainage, and incidence of atrial fibrillation were recorded for all patients.

Results: Preoperative NLR was significantly lower in Group 1 (P < 0.0001), and there was no significant difference between the groups in terms of postoperative NLR (P = 0.217) when the two groups were compared. The patients in Group 2 had a longer length of stay in the ICU (P = 0.035) and in the hospital (P = 0.034). There was a positive correlation between preoperative NLR and length of stay in the ICU (P = 0.017) and the hospital (P = 0.014). No statistically significant differences in postoperative drainage or incidence of postoperative atrial fibrillation were detected between the two groups.

Conclusion: The results of our study demonstrate that the postoperative NLR may be useful to predict the length of hospital and ICU stays and help the management of follow-up and treatment processes in patients undergoing CABG surgery.

Key words: Neutrophil/lymphocyte ratio, coronary artery bypass graft surgery, hospital stay, intensive care unit stay, atrial fibrillation

1. Introduction

Atherosclerosis and related complications are the most common cause of death worldwide. Coronary artery disease is one of the most important atherosclerotic vascular diseases. Coronary artery bypass grafting (*CABG*) is currently one of the most frequent surgical procedures performed with *low* periprocedural *mortality rates*. The morbidity associated with CABG is relatively high, however, with over a third of CABG procedures involving complications (1). Some of these complications may be attributed to inflammatory changes that occur during extracorporeal circulation (2). The changes that occur during the extracorporeal circulation of blood must be well known and the unknown aspects need to be investigated in detail (3).

Blood cells, plasma proteins, the complement system, and cytokines have effects on each other while these inflammatory changes occur. Contact with external surfaces activates the contact activation pathway. Kallikrein, one of the major components of this system, activates neutrophils. Activated neutrophils may cause inflammatory damage to organs and tissues by chemotactic stimulus. Also, cytokines and oxygen radicals released from neutrophils' granules may cause systemic inflammatory response characterized by symptoms such as hypotension, fever, and tachycardia/bradycardia. Monocytes and lymphocytes particularly cause strong inflammatory responses after making contact with external surfaces during cardiopulmonary bypass. These cytokines and some vasoactive substances cause hypotension and increased vascular permeability,

* Correspondence: dr-abdozer@hotmail.com

which leads to an increase in the effect of inflammation. Activation of these systems also activates certain steps of coagulation and anticoagulation cascade. Secondary organ damage during these processes affects the general performance of the patient, healing time, and short- and long-term postoperative results (4).

The neutrophil/lymphocyte ratio (NLR) is a simple parameter that is related to systemic inflammation and was first used by cardiologists to determine mortality risk after major cardiac events (5). NLR has also been used as an important prognostic criterion in some malignancies such as breast, kidney, esophagus, and lung cancers and as a responsive criterion for treatments of some diseases such as acute appendicitis and diabetes mellitus (6).

There are many studies that used NLR as an indicator of the inflammatory response, though there are not enough data about the effect of preoperative NLR on outcomes of CABG. The aim of this study is to determine the effect of preoperative NLR on the postoperative course of CABG surgery.

2. Materials and methods

This randomized prospective study was conducted with the approval of the Local Ethics Committee of Gazi University. Sixty-two patients aged between 41 and 80 years, scheduled for elective CABG surgery with ASA I–II risk and without a history of preoperative blood transfusion, were included in the study. Three patients were excluded due to their need for additional surgical procedures other than CABG. Two groups were formed based on NLR (cut-off value = 4) according to preoperative complete blood count results. Patients who had NLR lower than 4 formed Group 1 and those with NLR higher than 4 formed Group 2. Routine anesthetic procedures were performed depending on patients' clinical status. NLR values of routine blood samples taken after cardiopulmonary bypass were recorded. Postoperative data such as hospitalization and ICU stay times, chest tube drainage, and incidence of atrial fibrillation were recorded for all patients.

2.1. Administration of anesthesia

Patients were premedicated with 0.1 mg/kg subcutaneous morphine. Under standard ECG, with noninvasive blood pressure and SpO_2 monitorization, 1 mg/kg IV lidocaine was given, followed by 3 mg/kg sodium thiopental and 0.6 mg/kg rocuronium. After invasive monitorization of arterial (radial) blood pressure, thiopental was completed to 5–7 mg/kg depending on blood pressure, and 1 µg/kg remifentanil infusion was given per minute before endotracheal intubation. For the maintenance of anesthesia, 1 MAC isoflurane in a 40% O_2/air mixture and 0.1–0.5 µg/kg IV remifentanil infusion was given. In addition, 0.15 mg/kg rocuronium was given every 45 min. Ventilation parameters were 8 mg/kg tidal volume, 12 breaths/min, and 5 cm/H_2O PEEP. After intubation, a central venous catheter was inserted via the right internal jugular vein and a Foley catheter was inserted for measurement of urine output. Depending on hemodynamic parameters, dopamine, noradrenaline, and milrinone infusions were given. After surgery, patients were transferred to the ICU intubated with inotrope support. After 3–4 h, patients were extubated when they were hemodynamically and surgically stabile.

2.2. Statistical analysis

Statistical analysis data are presented as [mean ± standard deviation, median (min–max), n (%)]. In all calculations, the level of significance was accepted as $P < 0.05$. Using the Kolmogorov–Smirnov test, measured parameters were evaluated as to whether the distribution was normal or abnormal. In groups showing normal distribution, independent groups were evaluated to determine if there was a significant difference by using the Student t-test. In groups showing abnormal distribution, the Mann–Whitney U test was used. The correlation between hospitalization time and ICU stay time was evaluated by using the Pearson correlation test.

3. Results

Demographical data of the patients were similar (Table 1).

Preoperative NLR was significantly lower in Group 1 (2.3 in Group 1 and 5.8 in Group 2) ($P < 0.0001$). Postoperative NLR was similar between the groups ($P = 0.217$) (Table 2).

Length of stay in the ICU was significantly longer in Group 2 ($P = 0.035$). Similarly, length of hospital stay was also significantly longer in Group 2 ($P = 0.034$) (Table 2).

No statistically significant differences in postoperative drainage or incidence of postoperative atrial fibrillation were detected between the two groups. Postoperative drainage was 507.35 ± 182.85 mL in Group 1 and 614.95 ± 315.46 mL in Group 2. Four patients in Group 1 (10.8%) and 3 patients in Group 2 (13.6%) developed atrial fibrillation in the postoperative period (Table 2).

Preoperative and postoperative white blood cell count values were significantly higher in Group 2 when compared with Group 1 ($P < 0.0001$, $P = 0.001$). Duration of postoperative ventilation was 375.00 ± 59.34 min in Group 1 and 544.62 ± 219.11 min in Group 2 and it was found to be significantly higher in Group 2 ($P < 0.0001$). Postoperative need for inotropic drugs was significantly higher in Group 1 compared to Group 2 ($P = 0.019$) (Table 3).

A positive correlation was detected between preoperative NLR and both hospitalization time ($r = 0.227$, $P = 0.014$) and ICU stay time ($r = 0.220$, $P = 0.014$) (Table 4).

Table 1. Preoperative characteristics of the patients (mean ± SD, median (minimum–maximum), n (%))

	Group 1 (n = 37)	Group 2 (n = 22)	P-value
Age (years)	60.5 ± 8.1	62.9 ± 8.9	0.149
Sex (male/female)	22/15	15/7	0.099
Number of grafts	3 (1–5)	3 (1–5)	0.219
Hypertension	34 (91.9)	22 (100)	0.448
Diabetes mellitus	15 (40.5)	8 (36.4)	0.750
COPD	12 (32.4)	4 (18.2)	0.234
Hyperlipidemia	19 (51.4)	8 (36.4)	0.264

SD, Standard deviation; COPD, chronic obstructive pulmonary disease.

Table 2. Operative and postoperative data (mean ± SD, n).

	Group 1 (n = 37)	Group 2 (n = 22)	P-value
Preoperative NLR	2.3 ± 0.9	5.8 ± 1.0*	<0.0001
Postoperative NLR	10.4 ± 6.4	12.2 ± 8.5	0.217
CBP time (h)	1.8 ± 0.5	1.6 ± 0.5	0.117
Cross-clamp time (min)	67.04 ± 20.78	64.62 ± 20.60	0.733
ICU stay (days)	3.0 ± 1.3	4.5 ± 6.3*	0.035
Hospital stay (days)	7.7 ± 1.8	12.2 ± 18.4	0.034
Postoperative drainage (mL)	507.35 ± 182.85	614.95 ± 315.46	0.076
Postoperative cardiac rhythm (NSR/atrial fibrillation)	33/4	19/3	0.525

*P < 0.05 compared to Group 1; SD, standard deviation; NLR, neutrophil/lymphocyte ratio; CPB, cardiopulmonary bypass; ICU, intensive care unit; NSR, normal sinus rhythm.

Table 3. Preoperative and postoperative data (mean ± SD, n).

	Group 1 (n = 37)	Group 2 (n = 22)	P-value
Preoperative WBC count (/µL)	7746.62 ± 1684.35	11,373.75 ± 3756.92*	<0.0001
Postoperative WBC count (/µL)	10,521.15 ± 2368.28	14,383.75 ± 4520.20*	0.001
Preoperative Plt count (/µL)	244,923.08 ± 74,608.94	221,000.00 ± 80,970.20	0.236
Postoperative Plt count (/µL)	139,923.07 ± 33,436.02	141,750.00 ± 44,287.84	0.853
Preoperative SpO_2	94.92 ± 1.61	94.38 ± 3.01	0.351
Postoperative SpO_2	95.38 ± 3.54	96.87 ± 1.39	0.054
Ejection fraction (%)	53.58 ± 8.21	56.75 ± 5.99	0.087
Duration of postoperative ventilation (min)	375.00 ± 59.34	544.62 ± 219.11*	<0.0001
Urine output (mL)	2385.38 ± 655.56	2597.50±843.11	0.268
Postoperative need for inotropic drugs (n)	27	9*	0.019

*P < 0.05 compared to Group 1; SD, standard deviation; WBC, white blood cell; Plt, platelet; SpO_2, partial oxygen saturation.

Table 4. Correlation data between preoperative NLR and length of stay in hospital and ICU.

	r	P
ICU stay	0.220	0.017
Hospital stay	0.227	0.014

NLR, Neutrophil-lymphocyte ratio; ICU, intensive care unit.

4. Discussion

A number of studies have demonstrated the importance of NLR in treatment of coronary artery disease and the follow-up process after cardiac surgery. The effects of blood cells and mediators released from these cells to other body cells and certain body systems are being researched in detail (7–9). Aldemir et al. studied the changes of NLR in patients undergoing on-pump and off-pump CABG surgery (10). They stated that the influence of on-pump versus off-pump CABG surgery on changes in leukocyte counts after surgery was shown to be more prominent in the early stages after surgery. In another study, acute kidney damage risk after pump-requiring surgeries (CABG, valve replacement, ascending aorta replacement, etc.) was found related to increased postoperative NLR (5). Another study showed that there is a positive correlation between increased postoperative NLR and increased mortality rate in patients undergoing CABG above 45 years old (11). A different study implied that there is a significant relation between postoperative decreased saphenous vein graft patency and increased NLR, in addition to the necessity of evaluating other parameters while calculating risk of decreased patency (12).

In a study that evaluated long-term mortality, it was shown that increased NLR means increased short-term complications and increased long-term mortality. This study also recommended adding the NLR to the charts of risk scoring before cardiac surgery (13). A broadly based metaanalysis revealed that the increase of NLR after surgery may predict the risk of new-onset atrial fibrillation (14). Another study also showed the relation between increased NLR and atrial fibrillation after surgery (15).

A study of patients who had Stanford A type acute aortic dissection claimed that increased NLR is useful to predict short-term mortality along with other parameters (16). In a study evaluating patients with endocarditis, it was shown that increased NLR alone directly affects the symptoms of endocarditis and is a good predictor of prognosis (17). In a study of peripheral arterial diseases and cardiac diseases, it was found that increased NLR is a risk factor for long-term cardiovascular mortality in patients with peripheral arterial disease (18). One study found that the development of postpericardiotomy syndrome, an autoimmune reaction that can be seen in about 10%–40% of patients after cardiac surgery, can be predicted by measuring the postoperative NLR (19).

In a broadly based retrospective study including 444 patients it was shown that preoperative NLR is a predictor of saphenous vein graft patency in patients after CABG (20). Another study of 1938 patients found that increased preoperative NLR increased the risk of mortality after CABG and this prognostic utility was independent of the well-recognized individual risk factors and the EuroSCORE (21).

In our study, we have found a positive correlation between the preoperative NLR and the ICU ($P = 0.017$) and hospital stays ($P = 0.014$) after CABG surgery. Increased NLR is an important sign of onset and increase of inflammation. The results of our study demonstrate that the postoperative NLR may be useful to predict the length of hospital and ICU stays and help in the management of follow-up and treatment processes in patients undergoing CABG surgery. The increase in the postoperative NLR value when compared with the preoperative NLR may be the very first sign of many factors that could affect the recovery process.

References

1. Borst C, Gründeman PF. Minimally invasive coronary artery bypass grafting: An experimental perspective. Circulation 1999; 99: 1400-1403.
2. Vohra HA, Whistance R, Modi A, Ohri SK. The inflammatory response to miniaturised extracorporeal circulation: A review of the literature. Mediators Inflamm 2009; 2009: 707042.
3. Higgins RSD, Perez-Tamayo A. Kardiyopulmoner bypass eşliğinde koroner arter bypass cerrahisi. In: Kaiser LR, Kron IL, Spray TL, editors. Mastery of Cardiothoracic Surgery [Güngör A, Translator]. 2nd ed. Ankara, Turkey: Güneş Tıp Kitabevleri, 2013. pp. 437-440 (in Turkish).
4. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO 3rd, Criqui M, Fadl YY, Fortmann SP, Hong Y, Myers GL et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: a statement for health care professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation 2003; 107: 499-511.
5. Kim WH, Park JY, Ok SH, Shin IW, Sohn JT. Association between the neutrophil/lymphocyte ratio and acute kidney injury after cardiovascular surgery: a retrospective observational study. Medicine. 2015; 94: e1867.

6. Kahramanca Ş, Özgehan G, Şeker D, Gökce Eİ, Şeker G, Tunç G, Küçükpınar T, Kargıcı H. Neutrophil-to-lymphocyte ratio as a predictor of acute appendicitis. Ulus Travma Acil Cerr Derg 2014; 20: 19-22.

7. Kolackova M, Krejsek J, Svitek V, Kune, P, Mandak J, Holubcova Z, Lonsky V. The effect of conventional and mini-invasive cardiopulmonary bypass on neutrophil activation in patients undergoing coronary artery bypass grafting. Mediators Inflamm 2012; 2012: 152895.

8. Akbas H, Erdal AC, Demiralp E, Alp M. Effects of coronary artery bypass grafting on cellular immunity with or without cardiopulmonary bypass: changes in lymphocytes subsets. Cardiovasc Surg 2002; 10: 586-589.

9. Mazzeffi M, Lund L, Wallace K, Herrera AV, Tanaka K, Odonkor P, Strauss E, Rock P, Fiskum G. Effect of cardiopulmonary bypass on platelet mitochondrial respiration and correlation with aggregation and bleeding: a pilot study. Perfusion 2016; 31: 508-515.

10. Aldemir, M, Bakı ED, Adalı F, Çarşanba G, Tecer E, Taş HU. Comparison of neutrophil:lymphocyte ratios following coronary artery bypass surgery with or without cardiopulmonary bypass. Cardiovasc J Afr 2015; 26: 159-64.

11. Ay D, Erdolu B, Yumun G, Aydin U, Demir A, Tiryakioglu O, Vural AH. Comparing the effectiveness of neutrophil-lymphocyte ratio as a mortality predictor on middle and advanced age coronary artery bypass graft patients. Northern Clinics of Istanbul 2014; 1: 95-100.

12. Balta S, Demirkol S, Kurt O, Akhan M, Akgul EO, Kucuk U. Neutrophil–lymphocyte ratio is a predictor of saphenous vein graft patency in patients undergoing coronary artery bypass surgery. Clin Appl Thromb Hemost 2013; 20: 219-220.

13. Silberman S, Abu-Yunis U, Tauber R, Shavit L, Grenader T, Fink D, Bitran D, Merin O. Neutrophil-lymphocyte ratio: prognostic impact in heart surgery. Early outcomes and late survival. Ann Thorac Surg 2018; 105: 581-586.

14. Weymann A, Ali-Hasan-Al-Saegh S, Popov AF, Sabashnikov A, Mirhosseini SJ, Liu T, Tse G, Lotfaliani M, Ghanei A, Testa L et al. Hematologic indices as predictors of atrial fibrillation following isolated coronary artery bypass grafting, valvular surgery or combined procedures: A systematic review with meta-analysis. Kardiol Pol 2018; 76: 440-451.

15. Durukan AB, Gurbuz HA, Unal EU, Tavlasoglu M, Durukan E, Salman N, Ucar HI, Yorgancioglu C. Role of neutrophil/lymphocyte ratio in assessing the risk of postoperative atrial fibrillation. J Cardiovasc Surg (Torino) 2014; 55: 287-293.

16. Oz K, Iyigun T, Karaman Z, Çelik Ö, Akbay E, Akınc O, Erkanli K. Prognostic value of neutrophil to lymphocyte ratio and risk factors for mortality in patients with Stanford Type A aortic dissection. Heart Surg Forum 2017; 20: E119-E123.

17. Bozbay M, Uyarel H. Neutrophiltolymphocyte ratio: a novel and simple prognostic marker for infective endocarditis. J Crit Care 2015; 30: 822.

18. Erturk M, Cakmak HA, Surgit O, Celik O, Aksu HU, Akgul O, Gurdogan M, Bulut U, Ozalp B, Akbay E et al. The predictive value of elevated neutrophil to lymphocyte ratio for long-term cardiovascular mortality in peripheral arterial occlusive disease. J Cardiol 2014; 64: 371-376.

19. Sevuk U, Bilgic A, Altindag R, Baysal E, Yaylak B, Adiyaman MS, Akkaya S, Ay N, Alp V. Value of the neutrophil-to-lymphocyte ratio in predicting post-pericardiotomy syndrome after cardiac surgery. Eur Rev Med Pharmacol Sci 2016; 20: 906-911.

20. Tasoglu I, Turak O, Nazli Y, Ozcan F, Colak N, Sahin S, Kavasoglu K, Genc B, Sert D, Karahan M et al. Preoperative neutrophil-lymphocyte ratio and saphenous vein graft patency after coronary artery bypass grafting. Clin Appl Thromb Hemost 2014; 20: 819-824.

21. Gibson PH, Croal BL, Cuthbertson BH, Small GR, Ifezulike AI, Gibson G, Jeffrey RR, Buchan KG, El-Shafei H, Hillis GS. Preoperative neutrophil-lymphocyte ratio and outcome from coronary artery bypass grafting. Am Heart J 2007; 154: 995-1002.