



## **THE RELATIONSHIP BETWEEN NEUTROPHIL TO LYMPHOCYTE RATIO (NLR) WITH REHOSPITALIZATION AND MORTALITY IN PATIENTS WITH ACUTE CORONARY SYNDROME (ACS)**

Lesmana J<sup>1</sup>, Lefi A<sup>2</sup>

<sup>1</sup>General Practitioner, <sup>2</sup>Cardiologist Consultant at PHC Hospital, Surabaya City

### **Background**

Cardiovascular disease is still the leading cause of death globally and is expected to continue to increase. In Indonesia, ischemic heart disease is the main cause of morbidity and mortality based on Acute Coronary Syndrome (ACS) is a manifestation of coronary heart disease where there is decompensation of the heart due to narrowing or blockage of coronary arteries. Neutrophil to Lymphocyte Ratio (NLR) is a non-specific marker of inflammation which is simple, widespread, and affordable, and has predictive value, especially the incidence of ACS. NLR has the predictive value for the rehospitalization after the ACS incident and the mortality rate in ACS patients.

### **Objective**

This study aims to determine the relationship between NLR values with the incidence of rehospitalization and death in ACS patients.

### **Method**

This study is a single-center observational analytical study conducted in a retrospective cohort. The number of ACS research subjects obtained from January to December 2021 are 102 patients who are included. NLR data taken at the time of hospital admission were divided into 3 groups; low (<3), moderate (3-5), and high (>5), data on the incidence of rehospitalization who returned to treatment with reinfarction or ACS complications and mortality data during treatment were obtained through electronic medical records and then analyzed using SPSS version 23.0 program.

### **Results**

A total of 48 patients with ACS were found in the group with low NLR values (47%), 27 people with moderate NLR scores (26.5%), and 27 people with high NLR scores (26.5%). The highest number of deaths was found in the high NLR category and there was a strong relationship between NLR values and mortality in ACS patients with a statistically significant level of significance ( $P = 0.038$ ). The relationship between NLR and the incidence of rehospitalization was found in 3 people (0.3%) who were found in the low and moderate NLR categories and there was no significant relationship ( $P = 0.264$ ).

### **Conclusion**

The NLR value was associated with mortality during treatment, but was not associated with the incidence of rehospitalization in ACS patients. NLR examination is a supporting examination with a wide range of access, affordable and useful in predicting the prognosis of ACS patients.

**Keywords: NLR, Acute Coronary Syndrome, Mortality, Re-hospitalization.**



## References

1. Chen C, Cong BL, Wang M, Abdullah M, Wang XL, Zhang YH, et al. Neutrophil to lymphocyte ratio as a predictor of myocardial damage and cardiac dysfunction in acute coronary syndrome patients. Integrative Medicine Research [Internet]. 2018 Jun 1 [cited 2020 May 6];7(2):192–9. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6026362/>
2. M Santhi et al. Global status report on noncommunicable diseases 2014 : attaining the nine global noncommunicable diseases targets, a shared responsibility. Geneva: World Health Organization, Cop; 2014.
3. Budzianowski J, Pieszko K, Burchardt P, Rzeźniczak J, Hiczekiewicz J. The Role of Hematological Indices in Patients with Acute Coronary Syndrome. Disease Markers. 2017;2017:1–9.
4. Mboi N, Murty Surbakti I, Trihandini I, Elyazar I, Houston Smith K, Bahjuri Ali P, et al. On the road to universal health care in Indonesia, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet. 2018 Aug;392(10147):581–91.
5. Sunjaya AP, Sunjaya AF, Priyana A. Insights and challenges of indonesia's acute coronary syndrome telecardiology network: three year experience from a single center and in west Jakarta, Indonesia. IOP Conference Series: Materials Science and Engineering. 2019 May 2;508:012142.
6. Collet JP, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal (2021) 42, 1289-1367.
7. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal [Internet]. 2017 Aug 26;39(2):119–77. Available from: <https://academic.oup.com/eurheartj/article/39/2/119/4095042>
8. Zhang S, Diao J, Qi C, Jin J, Li L, Gao X, et al. Predictive value of neutrophil to lymphocyte ratio in patients with acute ST segment elevation myocardial infarction after percutaneous coronary intervention: a meta-analysis. BMC Cardiovascular Disorders. 2018 May 2;18(1).
9. Balta S, Celik T, Mikhailidis DP, Ozturk C, Demirkol S, Aparci M, et al. The Relation Between Atherosclerosis and the Neutrophil–Lymphocyte Ratio. Clinical and Applied Thrombosis/Hemostasis. 2015 Feb 9;22(5):405–11.



10. Bajari R, Tak S. Predictive prognostic value of neutrophil–lymphocytes ratio in acute coronary syndrome. *Indian Heart Journal*. 2017 Apr;69:S46–50.
11. Mikhael R, Hindoro E, Taner S, Lukito AA. Neutrophil-to-lymphocyte ratio for predictor of in-hospital mortality in ST-segment elevation myocardial infarction: a meta-analysis. *Medical Journal of Indonesia*. 2020 Jul 1;29(2):172–82.
12. Ji Z, Liu G, Guo J, Zhang R, Su Y, Carvalho A, et al. The Neutrophil-to-Lymphocyte Ratio Is an Important Indicator Predicting In-Hospital Death in AMI Patients. *Frontiers in Cardiovascular Medicine*. 2021 Sep 20;8.
13. Wang X, Fan X, Ji S, Ma A, Wang T. Prognostic value of neutrophil to lymphocyte ratio in heart failure patients. *Clinica Chimica Acta*. 2018 Oct; 485:44–9.
14. Bekler A, Erbag G, Sen H, E, Ozcan S. Predictive value of elevated neutrophil-lymphocyte ratio for left ventricular systolic dysfunction in patients with non-ST-elevated acute coronary syndrome. *Pakistan Journal of Medical Sciences*. 2014 Nov 24;31(1).
15. Arbel Y, Shacham Y, Ziv-Baran T, Laufer Perl M, Finkelstein A, Halkin A, et al. Higher Neutrophil/Lymphocyte Ratio Is Related to Lower Ejection Fraction and Higher Long-term All-Cause Mortality in ST-Elevation Myocardial Infarction Patients. *Canadian Journal of Cardiology*. 2014 Oct;30(10):1177–82.
16. Oncel RC, Ucar M, Karakas MS, Akdemir B, Yanikoglu A, Gulcan AR, et al. Relation of Neutrophil-to-Lymphocyte Ratio With GRACE Risk Score to In-Hospital Cardiac Events in Patients With ST-Segment Elevated Myocardial Infarction. *Clinical and Applied Thrombosis/Hemostasis*. 2013 Sep 27;21(4):383–8.
17. Hendsun, Firmansyah Y, Felicia, Julita E. Neutrophils- Lymphocytes Ratio (NLR) and Platelet-Lymphocytes Ratio (PLR) As Predictors of NSTEMI Events. *Journal of Biological Engineering Research and Review*. 2020, 7(1), 24-32.
18. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. *European Heart Journal*. 2021 Aug 27;42(36).
19. Wikananda G, Ariawan E, Husin M. The relationship between neutrophil to lymphocyte ratio (NLR) at admission and GRACE mortality risk score in acute myocardial infarction patient at Tabanan Regency Hospital in 2017. *Intisari Sains Medis*. 2019 Apr 1;10(1).
20. Wang Z, Wang J, Cao D, Han L. Correlation of neutrophil-to-lymphocyte ratio with the prognosis of non-ST-segment elevation in patients with acute coronary syndrome undergoing selective

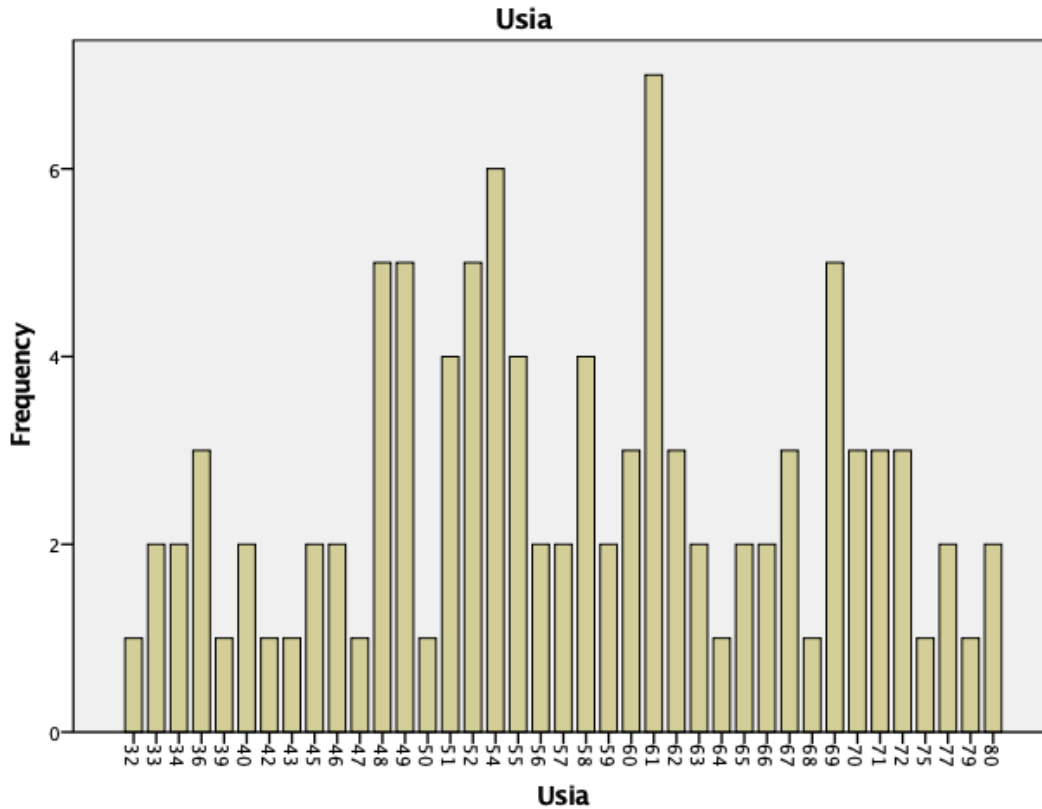


- percutaneous coronary intervention. *Journal of International Medical Research*. 2020 Oct;48(10):030006052095951.
21. He J. Neutrophil-to-lymphocyte ratio (NLR) predicts mortality and adverse-outcomes after ST-segment elevation myocardial infarction in Chinese people. Li J, Hao P, Hua Q, editors. *Int J Clin Exp Pathol* [Internet]. 2014 Jul 1;7(7):4045–56. Available from: [www.ijcep.com](http://www.ijcep.com) /ISSN:1936-2625/IJCEP0000818
  22. Wikananda G, Ariawan E, Husin M. The relationship between neutrophil to lymphocyte ratio (NLR) at admission and GRACE mortality risk score in acute myocardial infarction patient at Tabanan Regency Hospital in 2017. *Intisari Sains Medis*. 2019 Apr 1;10(1).
  23. Korkmaz A, Yildiz A, Gunes H, Duyuler S, Tuncez A. Utility of Neutrophil–Lymphocyte Ratio in Predicting Troponin Elevation in the Emergency Department Setting. *Clinical and Applied Thrombosis/Hemostasis*. 2014 Jan 14;21(7):667–71.
  24. Zhang S, Diao J, Qi C, Jin J, Li L, Gao X, et al. Predictive value of neutrophil to lymphocyte ratio in patients with acute ST segment elevation myocardial infarction after percutaneous coronary intervention: a meta-analysis. *BMC Cardiovascular Disorders*. 2018 May 2;18(1).
  25. Gazi E, Bayram B, Gazi S, Temiz A, Kirilmaz B, Altun B, et al. Prognostic Value of the Neutrophil–Lymphocyte Ratio in Patients With ST-Elevated Acute Myocardial Infarction. *Clinical and Applied Thrombosis/Hemostasis*. 2013 Jun 9;21(2):155–9.
  26. Curran FM, Bhalraam U, Mohan M, Singh JS, Anker SD, Dickstein K, et al. Neutrophil-to-lymphocyte ratio and outcomes in patients with new-onset or worsening heart failure with reduced and preserved ejection fraction. *ESC Heart Failure*. 2021 May 16;8(4):3168–79.
  27. Cho JH, Cho H-J, Lee H-Y, Ki Y-J, Jeon E-S, Hwang K-K, et al. Neutrophil-Lymphocyte Ratio in Patients with Acute Heart Failure Predicts In-Hospital and Long-Term Mortality. *Journal of Clinical Medicine*. 2020 Feb 18;9(2):557.
  28. Gul M, Uyarel H, Ergelen M, Ugur M, Isik T, Ayhan E, et al. Predictive Value of Neutrophil to Lymphocyte Ratio in Clinical Outcomes of Non-ST Elevation Myocardial Infarction and Unstable Angina Pectoris. *Clinical and Applied Thrombosis/Hemostasis*. 2012 Nov 8;20(4):378–84.



**Appendix**

**Lampiran 1. Tabel Deskriptif Subjek Penelitian**



**Jenis Kelamin**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Laki-Laki	83	81.4	81.4	81.4
Perempuan	19	18.6	18.6	100.0
Total	102	100.0	100.0	

**Diagnosis**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid STEMI	25	24.5	24.5	24.5
NSTEMI	3	2.9	2.9	27.5
UAP	74	72.5	72.5	100.0
Total	102	100.0	100.0	



**Kematian Selama Perawatan SKA**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Tidak	95	93.1	93.1	93.1
Ya	7	6.9	6.9	100.0
Total	102	100.0	100.0	

**Neutrophil to Lymphocyte Ratio**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid <3	48	47.1	47.1	47.1
3-5	27	26.5	26.5	73.5
>5	27	26.5	26.5	100.0
Total	102	100.0	100.0	

**Rehospitalisasi Paska Perawatan SKA**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Tidak	99	97.1	97.1	97.1
Ya	3	2.9	2.9	100.0
Total	102	100.0	100.0	

**Hipertensi**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Tidak	87	85.3	85.3	85.3
Ya	15	14.7	14.7	100.0
Total	102	100.0	100.0	

**Diabetes Mellitus**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Tidak	91	89.2	89.2	89.2
Ya	11	10.8	10.8	100.0
Total	102	100.0	100.0	



**Lampiran 2. Tabel Uji Hubungan NLR dengan Kematian Pada SKA**

**Symmetric Measures**

		Value	Asymptotic Standardized Error <sup>a</sup>	Approximate T <sup>b</sup>	Approximate Significance
Ordinal by Ordinal	Gamma	.710	.207	2.074	.038
Ordinal	Spearman Correlation	.243	.093	2.505	.014 <sup>c</sup>
Interval by Interval	Pearson's R	.253	.096	2.620	.010 <sup>c</sup>
N of Valid Cases		102			

- a. Not assuming the null hypothesis.
- b. Using the asymptotic standard error assuming the null hypothesis.
- c. Based on normal approximation.

**Lampiran 3. Tabel Uji Hubungan NLR dengan Rehospitalisasi Pada SKA**

**Symmetric Measures**

		Value	Asymptotic Standardized Error <sup>a</sup>	Approximate T <sup>b</sup>	Approximate Significance
Ordinal by Ordinal	Gamma	-.486	.381	-1.116	.264
Ordinal	Spearman Correlation	-.093	.070	-.929	.355 <sup>c</sup>
Interval by Interval	Pearson's R	-.096	.063	-.968	.335 <sup>c</sup>
N of Valid Cases		102			

- a. Not assuming the null hypothesis.
- b. Using the asymptotic standard error assuming the null hypothesis.
- c. Based on normal approximation.