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Prognostic Utility of the Combination of Monocyte-To-Lymphocyte Ratio and Neutrophil-To-Lymphocyte Ratio in Patients with NSTEMI

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Abstract **Original Research Article**

Inflammation plays a key role in the development of atherosclerosis and in the pathogenesis of acute coronary syndrome (ACS). Leukocytes and leukocytes ratios were recognized as inflammatory markers in predicting the presence and severity of ACS. This study aimed to evaluate prognostic value of the combination of monocyte-to-lymphocyte ratio (MLR) with ratio neutrophil-to-lymphocyte (NLR) for predicting long-term major adverse cardiac events (MACE) in patients with non-ST elevated myocardial infarction (NSTEMI), using data from cardiology department data of 183 patients with NSTEMI undergoing primary PCI between January 2018 and August 2021.

Keywords: acute coronary syndrome (ACS), (NSTEMI), Inflammation, Prognostic Utility.

INTRODUCTION

The neutrophil-to-lymphocyte ratio has been established as a cost-effective, feasible and reproducible inflammatory biomarker in many cardiovascular disorders, including acute coronary syndrome (ACS), angina pectoris and heart failure. Elevated NLR has been reported as an independent predictor of major adverse cardiac events in patients with ACS. The monocyte-to-lymphocyte ratio (MLR) has emerged as a novel systematic inflammatory marker related to increased cardiovascular risk. Recently, MLR has been reported to be associated with adverse clinical outcomes in various cardiovascular diseases.

OBJECTIVES

This study aimed to evaluate prognostic value of the combination of monocyte-to-lymphocyte ratio (MLR) with ratio neutrophil-to-lymphocyte (NLR) for predicting long-term major adverse cardiac events (MACE) in patients with non-ST elevated myocardial infarction (NSTEMI).

METHODS

Retrospective cohort study in the cardiology department in Mohamed VI university hospital center, Marrakesh, Morocco. Participants 183 patients with NSTEMI undergoing primary PCI between January 2018 and August 2021 were enrolled. The main outcomes were MACE. Data was analyzed using Microsoft excel software 2016.

RESULTS

According to the cut-off values of MLR 0.36 and NLR 2.15, the study population was classified into four groups: low MLR + low NLR group (n=111), low MLR + high NLR group (n=32), high MLR + low NLR group (n=19) and high MLR + high NLR group (n=21).

The high MLR + high NLR group had a lower MACE-free survival rate than the other three groups. Both MLR and NLR were independent predictors of long-term MACE. Moreover, the patients in the high MLR + high NLR group had for long-term MACE, with the low-MLR + low NLR group as reference.

Comparisons revealed that the combination of MLR with NLR achieved better performance in differentiating long-term MACE, compared with MLR, NLR, high-sensitivity C reactive protein, and had similar performance to all other combinations of the three biomarkers.

Table 1 Clinical outcomes between the four groups based on the cut-off values of MLR and NLR

Variable	Low MLR + low NLR (n=111)	Low MLR + high NLR (n=32)	High MLR + low NLR (n=19)	High MLR + high NLR (n=21)	P values
Follow-up 2years, n(%)	10 (9)	8 (25)*	5 (27.45)*	8 (38.09)* †‡	<0.001
All-cause death, n(%)	2 (1.8)	0	1 (5.26)	1 (4. 76)*	0.010
Cardiac death, n(%)	1 (0.9)	0	1 (5.26)	0	0.015
Non-fatal MI, n(%)	4 (3.6)	2 (6.25)	5 (26.31)*	2 (9.52)*	0.004
Stroke, n(%)	3 (2.7)	1 (3.12)*	0	1 (4.76)*	0.017

*Compared with the low MLR + low NLR group, p<0.05.
†Ccompared with the low MLR + high NLR group, p<0.05.
‡Compared with the high MLR + low NLR group, p<0.05.

DISCUSSION

Our results revealed that MLR was an independent predictor of long- term MACE and had comparable diagnostic ability as NLR for long-term MACE in patients with NSTEMI undergoing primary PCI. Compared with STEMI, NSTEMI is much more common and tends to have increased mortality in the year following MI [1]. Furthermore, we evaluated the combined usefulness of MLR and NLR for predicting long-term MACE in patients with NSTEMI undergoing primary PCI. Our results showed that the combination of MLR with NLR was an independent predictor, more predictive than individual markers, in predicting long-term MACE in patients with NSTEMI.

Lymphocytes are an integral part of the immune system, which participate in every phase of atherosclerosis. Lymphocytopenia, resulting from increased lymphocyte apoptosis, contributes to atherosclerotic plaque growth, lipid core development, plaque destabilisation, post infarct cardiac remodeling and progression [2]. Lower lymphocyte count was reported to be an early marker of acute myocardial infraction, and was associated with worse cardiovascular outcomes [3]. Obviously, it could be concluded that NLR, a composite marker of neutrophils and lymphocytes, can provide prognostic value in patients with ACS. In agreement with previous evidence, our study confirmed the prognostic role of increased NLR in patients with NSTEMI.

To date, just a few studies have attempted to elucidate the impact of MLR on cardiovascular disease. In our previous studies, MLR had the potential to assess coronary lesion severity, and identify the vulnerable plaques in patients with stable angina [4]. Siva *et al.*, [5] showed that increased MLR level was associated with higher mortality in patients with acute heart failure. Kiris *et al.*, [6] reported that elevated MLR level was independently associated with a higher risk of 6-month mortality in patients with STEMI undergoing primary PCI. Gijsberts *et al.*, [7] found that MLR significantly improved mortality prediction in patients with coronary angiography. Thus, a high MLR was associated with adverse cardiac clinical outcomes, though fewer studies have been performed for MLR and cardiac prognosis, compared with those for NLR.

Shumilah *et al.*, proved in their study that NLR was the strongest predictive marker of ACS, comparing with MLR, they recommend using NLR as a simple, inexpensive, and widely available inflammatory marker, which can be an auxiliary biomarker in the diagnosis of ACS [8].

CONCLUSION

In conclusion, the combined usefulness of MLR with NLR gains a prognostic value in patients with NSTEMI, which could be used to identify the high-risk patients with poor outcomes and adjust their treatment accordingly. These findings provide a new perspective on the non-invasive, simple, economical and feasible biomarkers in predicting long- term MACE in patients with NSTEMI.

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