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Research Article

Prognostic Importance of Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratios in Multiple Myeloma Patients

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Abstract

Objectives: To evaluate the prognostic significance of baseline neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in newly diagnosed multiple myeloma (MM).

Methods: We retrospectively analyzed 327 MM patients (2012–2018) from a single tertiary center. Baseline clinical, hematologic, and biochemical data were collected. NLR and PLR were calculated. OS was estimated via Kaplan–Meier and Cox regression. ROC analysis determined an NLR cutoff.

Results: Median OS was 46.1 months; 1-, 2-, and 5-year OS rates were 77.4%, 64.5%, and 44.0%, respectively. Each one-unit increase in NLR raised the risk of death by 9.3% (HR 1.093; p=0.015). NLR correlated with poorer OS in ISS stage II, hemoglobin <10 g/dL, ≥40% bone marrow plasma cell infiltration, and calcium ≥11 mg/dL. PLR showed no association with OS (p=0.957). ROC analysis identified an NLR cutoff of 1.7 (AUC 0.584).

Conclusion: Higher baseline NLR is associated with worse survival and adverse MM features but is insufficient as a standalone marker alongside ISS/R-ISS. PLR lacks prognostic value.

Keywords: Multiple myeloma, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, prognosis

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Multiple myeloma (MM) is a malignant plasma cell disorder that accounts for about 1–2% of all cancers and approximately 10–15% of hematologic malignancies.[1,2] The annual incidence in the United States is around 4–5 per 100,000 persons.[2] Almost all cases of MM are preceded by a premalignant clonal plasma cell disorder, monoclonal gammopathy of undetermined significance (MGUS).[3]

Several clinical and biological factors have been identified as important prognostic markers in MM. These include patient performance status, cytogenetic risk, serum lactate dehydrogenase (LDH) level, bone marrow plasma cell proliferation, and plasma cell leukemia. Advanced age, International Staging System (ISS) stage, C-reactive protein, serum creatinine, platelet count, and immunophenotypic plasma cell markers have also been associated with outcomes. Bone marrow biopsy, cytogenetic analysis, and fluorescence in situ hybridization (FISH) are integral to staging but are invasive and/or costly. Therefore, there is ongoing interest in simple, inexpensive, and non-invasive

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laboratory markers that could complement existing prognostic systems.[4]

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), derived from routine complete blood counts, have been proposed as markers of systemic inflammation and host immune status. Elevated NLR and PLR have been associated with poor outcomes in several solid tumors and some hematologic malignancies. In MM, data are more limited, and reported cutoff values vary.

In this retrospective study, we aimed to evaluate whether NLR and PLR at diagnosis are associated with overall survival in MM, to explore their relationships with established clinical and laboratory parameters, and to determine whether a clinically useful cutoff value for NLR could be identified.

In routine clinical practice, inexpensive markers derived from complete blood counts are appealing because they are universally available, rapidly reported, and do not require additional sampling. However, their interpretation in multiple myeloma is challenging due to frequent baseline cytopenias, renal dysfunction, and heterogeneity in disease burden at presentation. Therefore, evaluating NLR and PLR in a real-world cohort treated across an evolving therapeutic era may help clarify whether these indices provide clinically actionable information beyond established staging systems and readily available laboratory parameters.

Methods

Study Population and Inclusion Criteria

This retrospective study included patients diagnosed with MM between January 2012 and September 2018, according to IMWG criteria. Patients were required to have been diagnosed, treated, and followed at our center, with available baseline clinical and laboratory data.

Exclusion criteria at the time of diagnosis were acute infection, human immunodeficiency virus infection, chronic liver disease, collagen vascular disease, any previous or concomitant malignant neoplasm, primary or secondary thrombocytopenia, and chronic use of anti-inflammatory drugs. Because inflammatory indices can be influenced by non-myeloma conditions, we applied prespecified exclusion criteria to reduce confounding from acute infection, chronic inflammatory disease, and concomitant malignancy. Nevertheless, residual confounding is possible in retrospective datasets, particularly related to unmeasured comorbidities, corticosteroid exposure around diagnosis, and differences in supportive care. These considerations were taken into account when interpreting effect sizes and the clinical utility of the identified cutoff. Both deceased and surviving patients who met these criteria were included, resulting in a final cohort of 327 patients.

Our center is a tertiary university hospital that provides diagnostic workup, first-line therapy, and longitudinal follow-up for patients with plasma cell dyscrasias. Follow-up information was obtained from outpatient visit records, inpatient charts, and the hospital information system. Vital status and date of last contact were verified through the hospital registry, national death registry, and phone contact, when applicable, to minimize outcome misclassification.

Clinical and Laboratory Data

Demographic and clinical variables collected from hospital records included age at diagnosis, sex, vital status at last follow-up, follow-up duration, performance status according to the Eastern Cooperative Oncology Group (ECOG) scale, ISS stage, percentage of bone marrow plasma cell infiltration, treatment type (conventional chemotherapy vs. regimens containing immunomodulatory drugs and/or proteasome inhibitors), and autologous stem cell transplantation (ASCT) status.

Baseline hematologic parameters were defined as values obtained at the time of diagnostic evaluation and prior to initiation of anti-myeloma therapy. When multiple measurements were available within the diagnostic window, the sample closest to the date of diagnosis was selected. This approach aimed to capture the patient's inflammatory and immune status at presentation and to reduce variability introduced by supportive treatments or early therapeutic intervention.

Baseline laboratory parameters at diagnosis included hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), white blood cell (WBC) count, absolute neutrophil count, absolute lymphocyte count, platelet count, blood urea nitrogen (BUN), serum creatinine, estimated glomerular filtration rate (eGFR; calculated using the Modification of Diet in Renal Disease formula), serum calcium, albumin, albumin/globulin ratio, total protein, LDH, and β2 microglobulin. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, and PLR by dividing the platelet count by the absolute lymphocyte count.

Overall survival (OS) was defined as the time from the date of diagnosis to death from any cause or last follow-up for censored patients.

Statistical Analysis

Receiver operating characteristic (ROC) analysis was performed on continuous variables to determine cutoff points.

ROC curves were examined for the relationship between baseline NLR and PLR and survival outcomes. The optimal cutoff was defined as the value providing the best combination of sensitivity and specificity for OS.

The Shapiro–Wilk test was used to assess the normality of continuous variables. Non-normally distributed variables were compared between two groups using the Mann–Whitney U test. Spearman rank correlation analysis was used to assess relationships between continuous variables.

Survival probabilities were estimated using the Kaplan–Meier method, and hazard ratios (HRs) were calculated by univariable Cox proportional hazards regression. A p value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS for Windows, version 22.0 (IBM Corp., Armonk, NY, USA).

Missing data were handled using a complete-case approach for each analysis; the number of patients included in each model is reported where relevant. Given the retrospective design and the long study period, some laboratory variables were not available for all patients. No imputation was performed, and results should be interpreted with the awareness that missingness may not be completely at random.

Results

Baseline Characteristics

A total of 327 MM patients fulfilling the inclusion criteria were analyzed. Baseline characteristics and main treatment details are presented in Table 1.

The mean age at diagnosis was 60.04±11.03 years (range 29–85), and 54.7% of the patients were male. The mean follow-up duration was 32.80±25.04 months. At the time of analysis, 49.2% of the patients were alive. The estimated median OS was 46.06±6.85 months. The 1-, 2-, and 5-year OS rates were 77.4%, 64.5%, and 44.0%, respectively.

The mean hemoglobin level was 10.41±1.99 g/dL. The mean absolute neutrophil and lymphocyte counts were 4,460.6±2,049.9/μL and 2,159.6±1,069.2/μL, respectively, and the mean platelet count was 236,960±101,749/μL. The mean NLR was 2.49±1.78 (range 0.30–13.61), and the mean PLR was 132.30±86.07 (range 10.09–735.00).

Table 1. Baseline characteristics and main treatment details of the patients (n=327)

Variable	Minimum	Maximum	Mean	Standard deviation
Age at diagnosis (years)	29	85	60.04	11.03
Followup period (months)	1	80	32.80	25.04
Hemoglobin (g/dL)	5.3	16.5	10.41	1.99
MCV (μm^3)	61.8	109.3	90.11	7.23
MCH (pg/cell)	19.5	37.7	30.03	2.83
MCHC (g/L)	27.2	36.8	33.26	1.29
RDW (%)	11.5	30.8	16.49	2.87
Neutrophil count (μL)	1,000	13,130	4,460.60	2,049.88
Lymphocyte count (μL)	380	10,670	2,159.60	1,069.21
Platelet count (μL)	28,000	580,000	236,960.20	101,749.22
N/L ratio	0.30	13.61	2.49	1.78
P/L ratio	10.09	735.00	132.30	86.07
eGFR (mL/min/1.73 m^2)	2.60	160.00	68.24	35.64
Creatinine (mg/dL)	0.37	19.48	1.65	1.81
Albumin (g/dL)	1.60	5.12	3.48	0.69
Total protein (g/dL)	3.89	20.20	9.26	2.39
Albumin/globulin ratio	0.09	5.85	0.83	0.62
Calcium (mg/dL)	3.22	17.70	9.78	1.61
β2microglobulin (mg/L)	1.71	49.97	8.73	8.52
LDH (U/L)	81.00	824.00	221.96	101.25

MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red cell distribution width; N/L: Neutrophiltolymphocyte; P/L: Platelettolymphocyte; eGFR: Estimated glomerular filtration rate; LDH: Lactate dehydrogenase.

The mean eGFR was 68.24±35.64 mL/min/1.73 m^2; mean serum creatinine was 1.65±1.81 mg/dL; albumin was 3.48±0.69 g/dL; total protein was 9.26±2.39 g/dL; albumin/globulin ratio was 0.83±0.62; calcium was 9.78±1.61 mg/dL; β2 microglobulin was 8.73±8.52 mg/L; and LDH was 221.96±101.25 U/L.

The most common myeloma subtypes were IgG kappa (50.5%) and IgG lambda (30.0%), followed by IgA kappa (11.9%). ECOG performance status was 0–1 in 57.5% and 2–4 in 42.5% of patients. ISS stage I, II, and III were present in 19.6%, 28.1%, and 52.3% of cases, respectively. Overall, 82.6% of patients received regimens including immunomodulatory drugs and/or proteasome inhibitors, while 17.4% received conventional chemotherapy alone. ASCT was performed in 23.2% of patients (Table 2).

Table 2. ECOG performance status, ISS stage, plasma cell subtype, treatment and autologous stem cell transplantation status (n=327)

Variable	n	%
ECOG performance status		
0–1	188	57.5
2–4	139	42.5
ISS stage		
Stage I	64	19.6
Stage II	92	28.1
Stage III	171	52.3
Plasma cell subtype		
IgA kappa	39	11.9
IgA lambda	20	6.1
IgM kappa	1	0.3
IgM lambda	0	0.0
IgG kappa	165	50.5
IgG lambda	98	30.0
Nonsecretory	4	1.2
Treatment regimen		
Conventional chemotherapy	57	17.4
IMiD and/or proteasome inhibitorbased	270	82.6
Autologous stem cell transplantation		
Yes	76	23.2
No	251	76.8

ECOG: Eastern Cooperative Oncology Group; ISS: International Staging System; ImiD: Immunomodulatory drug.

Association of NLR and PLR with survival

In univariable Cox regression analysis, each one-unit increase in NLR increased the risk of death by 9.3% (HR 1.093; 95% CI 1.018–1.173; p=0.015) (Table 3). Changes in PLR had no significant effect on the relative risk of death (HR 1.000; 95% CI 0.998–1.002; p=0.957). Since PLR showed no prognostic significance, further correlation and survival analyses focused on NLR.

Subgroup analyses and correlations

In patients younger than 65 years, a significant correlation was observed between increasing NLR and mortality; each unit increase in NLR predicted a 12.9% increase in the risk of death (HR 1.129; 95% CI 1.016–1.255; p=0.024). In patients with hemoglobin <10 g/dL, each unit increase in NLR predicted a 24.3% increase in mortality (HR 1.243; 95% CI 1.074–1.440; p=0.004).

Regression analysis examining the impact of bone marrow plasma cell infiltration on mortality identified 40% as the optimal cutoff. In patients with bone marrow infiltration ≥40%, each unit increase in NLR predicted a 16.6% increase in the risk of death (HR 1.166; 95% CI 1.071–1.270; p<0.001), whereas no significant association was found in those with <40% infiltration (p=0.728).

NLR showed a very weak but significant positive correlation with serum creatinine (r=0.142; p=0.010) and LDH (r=0.139; p=0.012), whereas no significant correlations were found with eGFR (p=0.072) or β2 microglobulin (p=0.283).

When ISS stage and NLR were evaluated together, a significant association was observed only in ISS stage II. In this group, each unit increase in NLR predicted a 43.1% increase in the risk of death (HR 1.431; 95% CI 1.145–1.788; p=0.002); no significant association was detected in ISS I or III.

In patients treated with regimens containing immunomodulatory drugs and proteasome inhibitors, each unit increase in NLR predicted an 8.2% increase in mortality (HR 1.082; 95% CI 1.003–1.166; p=0.040), whereas no significant association was observed in the group treated with conventional chemotherapy alone (p=0.147). In patients

Table 3. Effect of neutrophiltolymphocyte (N/L) and platelettolymphocyte (P/L) ratios on risk of death (Cox regression analysis)

Variable	Coefficient (B)	Standard error	Wald χ^2	df	p value	Hazard ratio (HR)	95% CI for HR (lower–upper)
N/L ratio	0.088	0.036	5.973	1	0.015	1.093	1.018–1.173
P/L ratio	0.000	0.001	0.003	1	0.957	1.000	0.998–1.002

N/L: Neutrophiltolymphocyte; P/L: Platelettolymphocyte; CI: Confidence interval; df: Degrees of freedom.

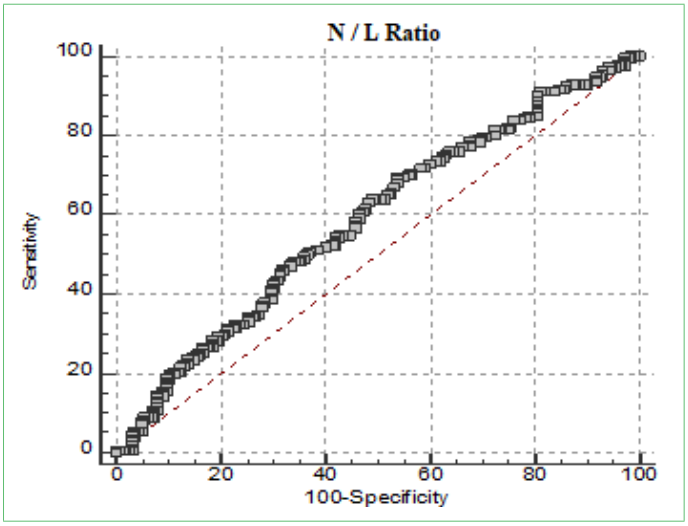

Figure 1. ROC curve of baseline neutrophiltolymphocyte ratio for predicting overall survival The optimal cutoff was N/L=1.7 (AUC 0.584; sensitivity 69.3%; specificity 46.0%).

with baseline calcium ≥11 mg/dL, each unit increase in NLR predicted a 30.4% increase in mortality (HR 1.304; 95% CI 1.042–1.632; p=0.040).

ROC analysis and NLR cutoff

ROC curve analysis was performed to determine an optimal cutoff for NLR in predicting OS (Fig. 1). Since PLR was not associated with survival, no cutoff for PLR was determined. The optimum cutoff for NLR, defined as the value providing the highest combined sensitivity and specificity, was 1.7. The AUC was 0.584 (95% CI 0.528–0.638; p=0.0078). At this threshold, sensitivity was approximately 69.3% and specificity 46.0% (95% CI 38.1–54.0). Thus, an NLR of 1.7 at diagnosis provides only weak clinical prediction for survival.

Discussion

In this retrospective study of 327 patients with multiple myeloma (MM), we investigated the prognostic significance of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) measured at diagnosis. The mean age at diagnosis was 60.04±11.03 years, and the mean follow-up duration was 32.80±25.04 months. The median overall survival (OS) was 46.06±6.85 months, with 1-, 2-, and 5-year OS probabilities of 77.4%, 64.5%, and 44%, respectively. At baseline, the mean NLR was 2.49±1.78, and the mean PLR was 132.30±86.07, indicating a wide distribution of systemic inflammatory status across the cohort.

Our main finding is that NLR at diagnosis shows a statistically significant but clinically modest association with overall survival, whereas PLR does not. In the entire cohort, each one-unit increase in NLR increased the risk of death by 9.3% (HR 1.093; 95% CI 1.018–1.173; p=0.015). By contrast, PLR had no significant effect on mortality (HR 1.00; 95% CI 0.998–1.002; p=0.957). These results support the hypothesis that an elevated NLR, reflecting a relative predominance of neutrophil-mediated inflammation over lymphocyte-mediated immune surveillance, is associated with poorer outcomes in MM, while PLR appears to be less informative in this setting.

The lack of association between PLR and survival in our cohort may reflect the multifactorial determinants of platelet counts in multiple myeloma, including marrow infiltration, treatment-related effects, bleeding risk, and inflammatory or infectious complications. Platelets can also be affected by renal dysfunction and nutritional status, which may dilute any direct relationship between PLR and tumor biology. Consequently, PLR may be a less stable proxy of systemic inflammation than NLR in this disease context.

From a biological standpoint, this is plausible. Neutrophils can promote tumor progression through pro-angiogenic cytokines, proteolytic enzymes, and growth factors, whereas lymphocytes are central to anti-tumor immunity. An increased NLR therefore suggests a shift toward a pro-tumor inflammatory milieu and impaired immune control.[4] Our findings are consistent with previous studies reporting adverse outcomes in MM patients with higher NLR values [5–7]. Onec et al.[5] found that NLR was predictive of survival in MM, Wongrakpanich et al.[6] and Li et al.[7] also reported prognostic associations of baseline NLR, though results for PLR were inconsistent, and Shi et al.[8] showed that elevated NLR and monocyte-to-lymphocyte ratio, together with decreased PLR, were associated with poor prognosis. Taken together, these data suggest that NLR is a reproducible, albeit not highly discriminative, prognostic marker in MM.

The modest AUC observed in our ROC analysis suggests that baseline NLR behaves more like a contextual risk correlate than a high-performing discriminative test. In other words, while NLR may capture aspects of host–tumor interaction and systemic stress, its overlap between survivors and non-survivors limits its use for individual-level decision-making at diagnosis. This emphasizes that statistically significant associations do not necessarily translate into clinically useful classification performance.

However, when we examined the discriminative performance of NLR using ROC analysis, the clinical utility appeared limited. The optimum cutoff point for NLR in predicting survival in our study was 1.7, yielding the highest combined sensitivity and specificity. At this threshold, sensitivity was approximately 70%, while specificity was only 46%, with an area under the ROC curve in the range of 0.528–0.638 (p=0.0078). Within the 95% confidence interval (38.1%–54.0% for specificity), NLR thus provides

only a weak prediction for clinical use at diagnosis. This is in contrast to some previous studies that proposed various cutoff values—1.72, 2.78, or 4.0—for NLR with stronger discriminative performance.[5,6,8] The differences may reflect variability in patient populations, treatment eras, and statistical methods, but they also underline that no universally accepted NLR cutoff has emerged for MM.

When we evaluated clinical and laboratory subgroups, NLR displayed differential associations with outcome:

- In patients with hemoglobin <10 g/dL, a one-unit increase in NLR predicted a 24.3% increase in the risk of death (HR 1.243; 95% CI 1.074–1.440; p=0.004), suggesting that NLR may be particularly relevant in patients with more advanced anemia and possibly higher disease burden.
- When bone marrow plasma cell infiltration was stratified at a 40% cutoff, no significant correlation between NLR and mortality was seen in patients with <40% infiltration (p=0.728), whereas in those with ≥40% infiltration, each one-unit increase in NLR predicted a 16.6% increase in mortality risk (HR 1.166; 95% CI 1.071–1.270; p<0.001).
- A significant association was also detected in patients with ISS stage II, where a one-unit increase in NLR increased the risk of death by 43.1% (HR 1.431; 95% CI 1.145–1.788; p=0.002). This suggests that NLR may capture additional risk particularly in intermediate-stage patients.
- Regarding renal and biochemical parameters, NLR showed a very weak but statistically significant positive correlation with creatinine (r=0.142; p=0.010) and LDH (r=0.139; p=0.012), while no significant correlation was observed with GFR (p=0.072) or beta-2 microglobulin (p=0.283).
- For hypercalcemia, we used a calcium level ≥11 mg/dL as a cutoff, consistent with established MM risk factors. In this subgroup, each one-unit increase in NLR was associated with a 30.4% increase in mortality risk (HR 1.304; 95% CI 1.042–1.632; p=0.040).

These subgroup findings indicate that NLR tends to be more prognostically informative in patients with markers of higher tumor burden or organ dysfunction (anemia, high marrow infiltration, elevated calcium, higher LDH, and impaired renal function), which is in line with the pathophysiology of MM.

Treatment-related analyses also yielded informative results. In our cohort, the majority of patients received regimens containing immunomodulatory drugs (IMiDs) and/or proteasome inhibitors (82.6%), while 17.4% received conventional chemotherapy alone; 23.2% underwent autologous stem cell transplantation (ASCT). In the group treated with IMiDs and proteasome inhibitors, a one-unit increase in NLR predicted an 8.2% increase in the risk of death attributable to poor treatment response (HR 1.082; 95% CI 1.003–1.166; p=0.040). No similar relationship was observed in the conventional chemotherapy group (p=0.147). These findings suggest that even in the era of novel agents, host-related inflammatory status, as reflected by NLR, may influence response outcomes and survival.

On the other hand, in patients who underwent ASCT, NLR did not show a significant difference in predicting OS compared with the non-transplant group (p=0.178). According to our results, NLR has no clear role in identifying candidates for autologous transplantation or in predicting post-transplant survival, which partially contrasts with studies that reported better post-transplant outcomes in patients with lower NLR values. [9–11]

The prognostic landscape of MM is further complicated by its well-recognized precursor state, monoclonal gammopathy of undetermined significance (MGUS), which precedes virtually all cases of MM. [3,12] Current MGUS and smoldering MM risk models rely on parameters such as M protein level, bone marrow plasma cell percentage, and free light chain ratio.[12] While we did not include MGUS or smoldering MM patients in our cohort, our results raise the broader question of whether inflammatory indices like NLR may play any role in identifying high-risk precursor states. This remains speculative and should be addressed in specifically designed prospective studies.

It is important to interpret these findings in the context of established prognostic systems. The International Staging System (ISS), based on serum β2 microglobulin and albumin,[13] and the Revised ISS (R-ISS), which additionally incorporates LDH and cytogenetic abnormalities, remain the standard tools for risk stratification in MM.[14,15] In our study, although NLR showed statistically significant associations with survival and several adverse clinical features, it did not add meaningful predictive value to staging beyond systems such as ISS and R-ISS. In other words, NLR appears to be a weak independent prognostic factor and does not substantially improve risk stratification when established markers are already taken into account.

From a practical standpoint, NLR can be viewed as a readily accessible marker that may raise clinical suspicion for higher-risk features when interpreted alongside anemia, renal impairment, LDH elevation, and hypercalcemia. However, our findings do not support using NLR alone to guide treatment intensity, transplant decisions, or counseling at diagnosis. Instead, NLR may be most appropriate as an adjunct variable in future composite scores that integrate established staging systems with routinely available laboratory data.

Our study has several limitations. First, it is a single-center, retrospective analysis, which may introduce selection bias and unmeasured confounding. Second, while the sample size of 327 patients is reasonable for a single-center study, it is still modest compared with large multicenter trials. Third, NLR and PLR were assessed only at baseline; we did not evaluate dynamic changes over time or during treatment, although studies performed at day +100 after ASCT suggest that post-treatment values may also be prognostically relevant.[9] Fourth, the ROC-derived cutoff for NLR in our cohort (1.7) showed weak discriminative power (p=0.078), suggesting that NLR alone is insufficient as a robust clinical decision-making tool at diagnosis. Finally, we did not incorporate R-ISS systematically due to the retrospective nature of the data and limitations in the availability of cytogenetic testing during the study period, which we acknowledge as a point of criticism.

Notable strengths of this study include the relatively large single-center cohort, consistent diagnostic criteria, and the inclusion of patients managed in a real-world setting where laboratory indices are routinely obtained. In addition, our analyses explored clinically relevant subgroups (e.g., anemia, marrow infiltration, calcium elevation), which may help clinicians understand in which scenarios NLR is more likely to reflect adverse disease biology.

Despite these limitations, our study contributes real-world data from a sizable, single-center cohort treated in the era of novel agents. It confirms that NLR is statistically associated with worse survival and with markers of higher tumor burden and organ dysfunction but, at the same time, demonstrates that its practical prognostic contribution is weak and does not replace or significantly enhance established staging systems. PLR, in contrast, did not show any independent prognostic value in our analysis.

Conclusion

In this retrospective cohort of 327 multiple myeloma patients, we found that:

- The baseline neutrophil-to-lymphocyte ratio (NLR) is statistically associated with overall survival; each one-unit increase in NLR increases the risk of death by approximately 9.3% (HR 1.093; 95% CI 1.018–1.173; p=0.015).
- The platelet-to-lymphocyte ratio (PLR) has no significant prognostic impact on survival (HR 1.00; 95% CI 0.998–1.002; p=0.957).
- The ROC-derived cutoff value of 1.7 for NLR provides weak discriminative power, with sensitivity around 70% but specificity of only 46% (AUC within 0.528–0.638; p=0.078), limiting its practical utility as a standalone prognostic marker at diagnosis.
- NLR shows stronger prognostic associations in subgroups with adverse clinical and laboratory features (hemoglobin <10 g/dL, bone marrow plasma cell infiltration ≥40%, ISS stage II, calcium ≥11 mg/dL, higher creatinine and LDH values), and among patients treated with IMiD- and proteasome inhibitor–containing regimens. However, NLR does not significantly influence survival after autologous stem cell transplantation and does not help in selecting transplant candidates.

Taken together, these findings indicate that while NLR reflects aspects of systemic inflammation and host–tumor interaction and is weakly prognostic, it does not meaningfully enhance staging or risk stratification when added to established systems such as ISS and R-ISS. PLR appears to be of no prognostic value in our cohort.

Given that bone marrow biopsy, cytogenetic and FISH analyses, and advanced imaging recommended by the International Myeloma Working Group are invasive and/or costly,[13,14] simple and inexpensive indices such as NLR and PLR are attractive in principle. However, based on our results, baseline NLR should currently be regarded as an auxiliary marker with limited clinical impact rather than a primary tool for risk-adapted treatment decisions in MM. PLR cannot be recommended as a prognostic marker in this context.

We recommend that future prospective, multicenter studies with larger patient numbers and standardized methodology:

- further investigate the prognostic value of NLR and other inflammatory indices,
- explore dynamic changes in these ratios during treatment (e.g., at day +100 post-ASCT),

and evaluate combined models that integrate inexpensive hematologic and biochemical ratios with established staging systems and modern biomarkers, from precursor states such as MGUS through to symptomatic MM.[14,15]

Such research may clarify whether more robust cutoff points or composite scores derived from routine laboratory tests can provide clinically meaningful prognostic information and contribute to truly individualized management strategies in multiple myeloma.

Disclosures

Ethics Committee Approval: The study was approved by the Gaziantep University Clinical Research Ethics Committee and was conducted in accordance with the Declaration of Helsinki.

Informed Consent: Written consent was obtained from all participants.

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