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RESEARCH ARTICLE

The Role of Inflammatory and Nutritional Indices as a Predictive Markers in Multiple Myeloma Patients in the Egyptian Population

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Abstract

Purpose: Multiple myeloma (MM) is a malignant proliferation of plasma cells which lead to a profound health affection. **Materials and Methods:** 130 NDMM patients were included in this retrospective analysis. Patients' clinico-pathological parameters, seven nutritional and inflammatory parameters were particularly noteworthy for investigation and correlation with disease stage, patient survival, and outcome. **Results:** 53 patients (40.8%) were female, 77 patients (59.2%) were male, and the median patient age was 56.5 (47.8-64.0) years. High TLC count, pronounced anemia, and rouleaux development were all statistically significantly associated with R/ISS stage III (P=0.003), P=0.001), and P=0.010), respectively. Serum creatinine levels, low eGFR, elevated LDH, hypoalbuminemia, elevated phosphate, elevated B2 microglobulin were all significantly correlated with R/ISS stage III (P=0.001), (P=0.001), (P=0.001), (P=0.001), (P=0.001), and (P=0.002), (P=0.001), (P=0.001), respectively. The analysis of inflammatory and nutritional indices revealed that R/ISS stage I is linked to low NLR, high PNI index, and high AAPR (P=0.013), (P=0.021), and (P=0.027), respectively, while R/ISS stage III is linked to an elevated iP/L ratio (P=0.014). Low PLR is also linked to R/ISS stage III, however the difference was not statistically significant. Following a 21-month follow-up, the cumulative OS is 37.7%, and the median OS is 29.2 months with 95% CI (22.65-35.75). Patients with low PNI and those with high NLR have worse OS (P=0.014 and P=0.029), respectively. Cox regression Multivariate analysis showed that elevated NLR is considered an independent predictor of worse overall survival. **Conclusion:** The study findings highlight the prognostic relevance of systemic inflammation and nutritional status in survival outcomes of NDMM patients

Keywords: Multiple Myeloma- Prognosis- Inflammatory indices- CBC

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Introduction

Multiple myeloma (MM) is a malignant neoplasm of plasma cells derived from a clonal expansion in the bone marrow (BM), characterized by bone destruction, renal failure, anemia, and hypercalcemia [1]. The Revised International Staging System (R/ISS) is the most widely accepted prognostic scoring system for patients with Newly diagnosed Multiple Myeloma (NDMM), which includes the former ISS staging system in addition to lactate dehydrogenase (LDH) levels and adverse cytogenetic aberrations (CA) [2]. A novel Staging system for myeloma has been developed and validated RW/ISS (Real World International Staging System) to include some specific cytogenetic and molecular aberrations like del (17p), t (14;16), in addition to the former revised staging system items [3].

Peripheral blood biomarkers related to inflammation may serve as prognostic indicators for MM [4]. Some studies showed that indices such as neutrophil-lymphocyte

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ratio (NLR) and monocyte-lymphocyte ratio (MLR) are tied to survival outcomes in MM patients [5-8]. Many studies report the close relationship between systemic inflammation and cancer with the study of C-reactive protein (CRP), albumin, the NLR (Neutrophil lymphocyte ratio), platelet-lymphocyte ratio (PLR), and others were of high notice of interest [9, 10].

We investigated the AMC (absolute monocyte count), iP/L (inverse platelet/ lymphocyte ratio, NLR, MLR, P/LR, AAPR (Albumin/Alkaline Phosphatase Ratio), and PNI (Prognostic Nutritional Index). Peripheral blood (AMC) is thought to reflect the bone marrow microenvironment. Abnormal AMC was also associated with inferior OS independent of validated prognostic markers, including the international staging system and lactate dehydrogenase [11, 12].

Also, platelet count may be related to inflammatory response in cancer patients, and reactive thrombocytosis is associated with poor survival outcomes in several types of cancer [13-15]. High P/LR was associated with poor prognosis in many types of cancers including MM [16-18]. The NLR is considered worthy of notice as it is a marker of systemic inflammation. The NLR has been reported to have prognostic value in patients with lymphoma or MM [11]. (MLR) is an inflammatory index in the studies of cancer, tuberculosis, and autoimmune diseases, and was associated with survival outcomes in MM patients [18]. Low AAPR was associated with survival outcomes and poor prognosis in NDMM [19]. Also, low PNI suggested poor prognosis and was an independent prognostic factor in patients with NDMM [20, 21].

We aimed to identify the value of inflammatory markers as a prognostic biomarker in NDMM patients and to assess their relation to patient outcomes.

Materials and Methods

In this retrospective study, we investigated 130 NDMM patients between July 2020 and October 2022, admitted to the Medical Oncology Department, NCI, Cairo University. The diagnosis of NDMM patients was established according to the WHO 5th edition of myeloid and lymphoid neoplasm [22]. This study was approved by the Institutional Review Board of the National Cancer Institute in accordance with the Declaration of Helsinki number CP2405-303-025. All baseline data were obtained from patients' records including demographic data (e.g., date of diagnosis, age, sex, last follow-up, survival status, and treatment protocols). Laboratory data including complete blood count (CBC), kidney function tests and biochemical tests in the form of serum creatinine, urea and calcium, serum albumin, serum lactate dehydrogenase (LDH), beta2 microglobulin (β2m), serum protein electrophoresis (E/P) and immunofixation (IF), bone marrow aspiration and assessment of bone marrow plasma cells (BMPC).

Seven inflammatory indices were calculated as follows, (MLR) = AMC/ALC, (NLR) = ANC/ALC, (PLR) =P/ALC, (PNI) =albumin (g/L) + 5 × ALC (10^9/L), (AAPR) = albumin (g/L)/ALP (μ/L), (AMC) and (iP/L). The best cutoff values of the above variables were as follows: MLR (0.53), NLR (1.09), PLR (55), PNI (34.4), AAPR (0.4), AMC (0.2), iP/L (1.95) [19].

Data were analyzed using SPSS win statistical package version 25 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. For quantitative data, comparison between two groups was done using student t-test. All tests are two tailed and a p-value ≤ 0.05 was considered significant. Bivariate correlation analysis was done to examine the relationship between two numeric data. The Pearson correlation (R) indicates: Strength of the relationship (strong or weak) and direction of the relationship: Positive (direct): variables move in the same direction, Negative (inverse): variables move in opposite direction. The interpretation of correlation: From 0 to 0.25 (– 0.25): no or little relationship from 0.25 to 0.50 (- 0.25 to – 0.50) fair degree of relationship, from 0.50 to 0.75 (–0.50 to – 0.75) moderate to good relationship, greater than 0.75 (or – 0.75): very good to excellent relationship.

Results

The Median patient age was 56.5 (47.8-64.0) years, of whom fifty-three patients (40.8%) were females and 77 (59.2%) were males. Regarding the R/ISS staging system, 68 (52.3%) were encountered in stage II, while stage I and stage III were represented with 46 (35.4%) and 48 (36.9%), respectively.

Regarding patients' demographic and laboratory data are Illustrated in Table 1.

The base line data of the inflammatory indices with specific cutoffs are presented in Table 2.

Regarding R/ISS correlations with patients' laboratory data, there were statistically significant associations between stage III (R/ISS) with high TLC count, marked anemia, and rouleaux formation with a mean of (9.94±6.90), (8.60±1.59), and 26 (89.7%) (P=0.003), (P=0.001), and (P=0.010), respectively. High eosinophil% and basophil% counts were found to be significantly associated with stage I (R/ISS), with a mean (2.43±3.21), (0.59±0.88), (P=0.041) and (P=0.006) respectively. Stage III R/ISS was also significantly associated with elevated serum creatinine levels, low eGFR levels,

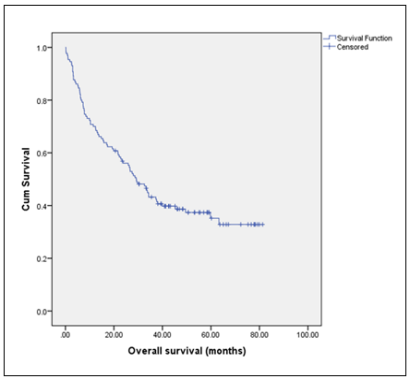

Figure 1. Kaplan-Meier Curve Showing Overall Survival (months) in Patients' group

Table 1. Clinicopathological Baseline Parameters among the Study Group

Clinical Data	Total (n=130) (%)
Age "years"	
Mean±SD	55.73±11.17
Gender	
Female	53 (40.8)
Male	77 (59.2)
ISS stage	
I	46 (35.4)
II	36 (27.7)
III	48 (36.9)
R/ISS stage	
Stage I	33 (25.4)
Stage II	68 (52.3)
Stage III	29 (22.3)
Osteolytic lesions	
Yes	95 (73.1)
No	24 (18.5)
CBC parameters (Mean±SD)	
TLC (x10^3/uL)	8.02±4.51
HB g/dl	10.06±2.46
Platelets (x10^3/uL)	238.36 ± 101.90
Neutrophils (%)	59.97 ± 12.55
ANC (x10^3/µL)	4.76 ± 2.53
Lymphocytes (%)	28.91 ± 11.09
ALC (x10^3/µL)	2.23 ± 1.63
Monocytes (%)	8.73 ± 6.04
AMC (x10^3/µL)	0.63 ± 0.39
Kidney function and chemistry tests (Mean±SD)	
Serum Calcium (mg/dL)	9.74 ± 1.96
Urea (mg/dL)	58.17 ± 39.06
Creatinine (mg/dL)	1.70 ± 1.65
<2 mg/Dl	100 (76.9)
≥2 mg/Dl	30 (23.1)
eGFR (mL/min/1.73m^2)	63.65 ± 33.22
LDH (U/L)	282.58 ± 182.70
<233g/Dl	93 (71.5)
>233g/Dl	37 (28.5)
Albumin (g/dL)	3.59 ± 0.79
<3.5 g/Dl	57 (43.8)
>3.5 g/Dl	73 (56.2)
B2 microglobulin (mg/L)	6.90 ± 5.18
<3.5 mg/L	49 (37.7)
≥3.5 mg/L	81 (62.3)
Phosphate (mg/dL)	3.88 ± 0.95
Alkaline phosphatase (U/L)	102.31 ± 53.43

TLC: total leucocyte count, Hb: hemoglobin, ANC: absolute neutrophil count, ALC: absolute lymphocyte count, AMC: absolute monocyte count, eGFR: estimated glomerular filtration rate, LDH: lactate dehydrogenase.

elevated LDH levels, hypoalbuminemia <3.5 g/dL and increased phosphate levels with a median 1.8 (1.1-3.2), 39.0 (19.0-64.0), 450.0 (305.5-578.0), 20 (69.0%), 5.0 (4.3-5.2), (P=0.001), (P=0.001), (P=0.001), (P=0.001) and (P=0.002) respectively. Stage II & III R/ISS were associated significantly with elevated levels of B2 microglobulin, with a median of 4.7 (3.3-9.3) and 10.0 (7.4-14.6) (P=0.001), while stage III R/ISS showed increased B2micr level ≥3.5 mg/L in [29] 100% of patients (P=0.001). The rest of the laboratory investigations and their correlation with R/ISS are listed in Table 3.

The bone marrow examination of NDMM patients included the cellularity, plasma cells, and hematopoiesis. Increase plasma cells were significantly associated with stage II/III R/ISS, with a mean of 17.0 (4.3-38.0) and 33 (12.5-56.5), respectively (P=0.003). The correlation of R/ISS and bone marrow examination is detailed in Table 4.

Regarding the association between the inflammatory indices and myeloma staging

There was a statistical association between R/ISS and iPLR ratio inflammatory index, where 20 (60.6%) patients' R/ISS stage I was associated with low iPLR at a cutoff <1.95, while R/ISS stage III was associated with increased iPLR ratio at cutoff >5.84, 5 (17.2%) vs. 10 (14.7%) R/ISS stage II respectively (P=0.014). R/ISS stage I was associated with low NLR at cutoff ≤2.57, 27 (81.8%), vs. 35 (51.5%) & 18 (62.1%) in stage II, and III, respectively (P=0.013).In the study of PLR results showed that R/ISS stage III was associated with low PLR (100%), however the difference was statistically not significant.

R/ISS stage I was associated with high PNI index, where medians of PNI stage I was 164.3 (134.1-195.5) vs. 153.4 (122.1-184.8) & 133.8 (93.1-164.8) in stage III and II respectively (P=0.021). Moreover, high AAPR inflammatory index, was statistically associated with R/ISS stage I (63.6%) at a cutoff >0.4, whereas stage II 44 (64.7%) and III 16 (55.2%) were associated with low AAPR index at a cutoff ≤0.4, and this relation was statistically significant (P=0.027). The rest of the inflammatory indices associations with R/ISS are discussed in Table 5.

Survival analysis

After a follow-up period of 21 months, survival analysis of the patient cohort showed that the median

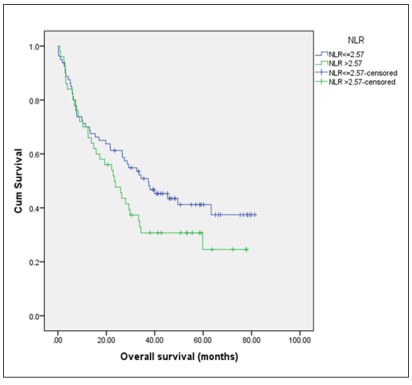

Figure 2. Kaplan-Meier Survival Curves in NLR Inflammatory Index.

Table 2. Inflammatory Indices Baseline Distribution among Study Group

Inflammatory indices	Total (n=130) (%)
AMC (x10^3/µL)	
<0.2	2 (1.5)
0.2-1	116 (89.2)
1-1.25	4 (3.1)
>1.25	8 (6.2)
iPLR	
<1.95	49 (37.7)
1.95 - 2.58	22 (16.9)
2.59 -3.75	27 (20.8)
3.76 -5.84	15 (11.5)
>5.84	17 (13.1)
MLR	
≤0.53	110 (84.6)
>0.53	20 (15.4)
NLR	
≤2.57	80 (61.5)
>2.57	50 (38.5)
PLR	
≤55	118 (90.8)
>55	12 (9.2)
AAPR	
≤0.4	72 (55.4)
>0.4	58 (44.6)
PNI (Mean±SD)	145.50±53.7

overall survival was 29.2 months, with a 95% CI (22.65-35.75). The cumulative overall survival (OS) through the follow-up was 37.7%, as shown in Figure 1.

The statistical associations between the studied inflammatory indices and patients' overall survival revealed that there was a statistically significant difference among patients with NLR groups, where those with high NLR >2.57 showed inferior overall survival than low NLR <=2.57 (P=0.014) as demonstrated in Figure 2. Moreover, there was a statistically significant difference regarding PNI groups where patients with high PNI >150 showed improved overall survival compared to patients with low PNI <150 (P=0.029), as shown in Figure 3. There were no statistically significant differences regarding survival outcomes in AMC, iP/L, MLR, PLR and AAPR inflammatory indices.

Univariate and Multivariate Cox Regression Analysis for Overall Survival.

In univariate Cox regression analysis, elevated NLR (>2.57) was significantly associated with worse overall survival (HR 1.832, 95% CI 1.126–2.981, p=0.015), and low PNI (≤150) also predicted poorer survival (HR 1.674, 95% CI 1.032–2.714, p=0.037). Other variables including AMC (≥1 vs <1, HR 1.478, 95% CI 0.912–2.393, p=0.110), iP/L ratio (>2.58 vs ≤2.58, HR 1.215, 95% CI 0.784–1.882, p=0.380), MLR (>0.53 vs ≤0.53, HR 0.958, 95% CI 0.553–1.659, p=0.890), PLR (>55 vs ≤55, HR 1.037, 95% CI 0.578–1.859, p=0.912), and AAPR (≤0.4 vs >0.4, HR 1.293, 95% CI 0.825–2.028, p=0.260) did not show significant prognostic impact.

Multivariate analysis adjusted for age, R/ISS stage, AMC, iP/L ratio, MLR, NLR, PLR, PNI, and AAPR confirmed that elevated NLR remained an independent predictor of worse overall survival (HR 1.710, 95% CI 1.045–2.800, p=0.031), while low PNI showed borderline significance (HR 1.592, 95% CI 0.980–2.580, p=0.059) as presented in Tabe 6.

These findings highlight the prognostic relevance of systemic inflammation and nutritional status in survival outcomes of this patient cohort, consistent with previously published data.

Discussion

MM, the second most common malignant hematological neoplasm is an incurable cancer [23, 24]. A higher disease burden may be the cause of the significant anemia and leucocytosis, elevated serum creatinine, low eGFR, elevated LDH, hypoalbuminemia, and elevated phosphate levels observed in our group of patients with advanced disease stages. cytokines release in response to inflammation, immunoglubulin-induced renal discomfort, etc [25]. According to a thorough analysis of the tumor microenvironment, inflammation is essential to the development, progression, and incidence of tumors [26]. By promoting tumor cell growth, development, angiogenesis, and metastasis, inflammatory cells found in the tumor microenvironment are known to play a role in this process. Furthermore, cancer patients' proinflammatory cytokines and chemokines directly contribute to the spread of the disease and increase resistance to anti-cancer treatment [27]. In other words, the ratios of proinflammatory to anti-inflammatory cytokines in cancer patients may influence the degree of protumorous inflammation [4]. Relationship between inflammation and cancer has been investigated in many studies [5, 19, 28].

To address the potential correlation of those inflammatory indices to tumor burden, staging, progression, and patient outcome, we examined potential, easily accessible, and calculable laboratory inflammatory and nutritional markers derived from blood tests that are

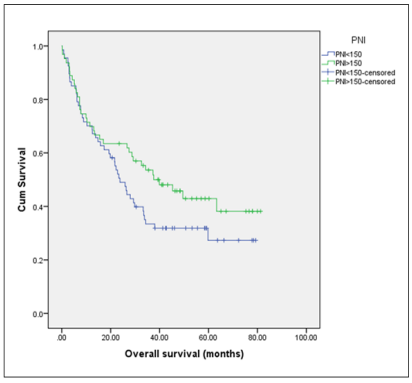

Figure 3. Kaplan-Meier Survival Curves in PNI Inflammatory Index.

Table 3. Association between R/ISS Stage and Clinicopathological Examination

	R/ISS stage			Test value	p-value
	Stage I (n=33)	Stage II (n=68)	Stage III (n=29)		
Age "years"					
Mean±SD	53.52±12.32	56.96±10.76	55.38±10.69	1.199	0.549
Gender					
Female	12 (36.4%)	29 (42.6%)	12 (41.4%)	0.369	0.832
Male	21 (63.6%)	39 (57.4%)	17 (58.6%)		
ISS stage					
I	32 (97.0%)	14 (20.6%)	0 (0.0%)	123.922	0.001
II	1 (3.0%)	35 (51.5%)	0 (0.0%)		
III	0 (0.0%) C	19 (27.9%) B	29 (100.0%) A		
Osteolytic lesions					
No	6 (18.2%)	13 (19.1%)	5 (17.2%)	7.329	0.12
Yes	25 (75.8%)	52 (76.5%)	18 (62.1%)		
Missed	2 (6.1%)	3 (4.4%)	6 (20.7%)		
CBC parameters (Mean±SD)					
TLC	7.99±3.07	7.22±3.53	9.94±6.90	11.612	0.003
Hb.	11.33±2.56 A	10.06±2.39 B	8.60±1.59 C	19.883	0.001
PLTS	303.30±94.18	218.87±86.91	210.17±113.64	19.064	0.001
Neut%	56.69±10.70 B	63.56±11.45 A	55.42±14.69B	10.657	0.005
ANC	4.31±1.65	4.83±3.03	5.09±2.04	2.769	0.25
Lym%	31.41±9.42	26.34±10.92	32.07±12.09	7.464	0.024
ALC	2.27±1.06	1.84±1.00	3.10±2.73	11.304	0.004
Mono%	8.85±2.51	9.15±7.90	7.62±3.29	2.985	0.225
AMC	0.62±0.32	0.60±0.40	0.72±0.44	3.603	0.165
Kidney function and chemistry tests					
Serum Ca	9.51±1.42	9.46±1.60	10.66±2.83	2.985	0.225
Urea	45.37±30.40	59.19±44.65	67.89±29.96	12.103	0.002
Creatinine	1.19±0.78	1.71±1.95	2.27±1.46	13.706	0.001
eGFR	76.85±30.80	65.13±30.95	45.17±33.83	15.506	0.001
LDH	165.00±94.51	267.97±176.48	450.62±151.62	44.849	0.001
LDH <233g/dL	32 (97.0%)	51 (75.0%)	10 (34.5%)	30.44	0.001
LDH>233g/dL	1 (3.0%)	17 (25.0%)	19 (65.5%)		
Albumin	4.12±0.52 A	3.49±0.80 B	3.23±0.72 C	24.539	0.001
Alb. <3.5 g/dL	3 (9.1%)	34 (50.0%)	20 (69.0%)	24.668	0.001
Alb >3.5 g/dL	30 (90.9%)	34 (50.0%)	9 (31.0%)		
B2 microdlobulin	2.40±0.48	6.57±5.01	11.08±4.26	52.354	0.001
B2micr <3.5 mg/L	26 (78.8%)	23 (33.8%)	0 (0.0%)	41.707	0.001
B2micr ≥3.5 mg/L	7 (21.2%)	45 (66.2%)	29 (100.0%)		
Phospahte	4.19±0.49	3.55±0.95	4.77±0.56	12.857	0.002
Alkaline phosphatase	93.31±28.51	112.56±56.73	90.89±61.81	5.612	0.06

routinely administered to the patients during admission.

It has been demonstrated that inflammatory markers can forecast the course of several malignancies, such as NDMM, cervical cancer etc [29-31].

Several studies have looked at how PLR affects both hematologic and non-hematologic cancers, and they have found that high PLR has a detrimental impact on survival and is linked to a bad prognosis. The systemic inflammatory response is known to be linked to reactive thrombocytosis [32-34]. Several studies found that M.M patients with low platelet counts are more likely to experience bleeding and hence worse prognosis [18, 35]. We found like others that decreased PLR and platelet count were linked to aggressive myeloma stage, which can be explained by either a relatively low platelet level or an elevated lymphocyte count. Increased lymphocyte counts signify the emergence of inflammation, which could reflect the poor course of MM in which a higher burden of marrow myeloma inhibits thrombopoiesis. In addition to MM's physical characteristics, inflammatory cytokines are thought to play a role in the disease's reduced thrombopoiesis. For instance, it has been demonstrated that transforming growth factor-β1, released by malignant plasma cells and mediates their proliferation

Table 4. Association between R/ISS Stage and BMA Examination

BMA examination	R/ISS stage			Test value	p-value
	Stage I (n=33)	Stage II (n=68)	Stage III (n=29)		
BMA Cellularity					
Hypercellular	14 (42.4%)	26 (38.2%)	9 (31.0%)	6.537	0.587
Hypocellular	1 (3.0%)	9 (13.2%)	6 (20.7%)		
Normocellular	16 (48.5%)	30 (44.1%)	12 (41.4%)		
Not done	0 (0.0%)	1 (1.5%)	0 (0.0%)		
Missed	2 (6.1%)	2 (2.9%)	2 (6.9%)		
BMPCs (Mean±SD)	17.42±26.78	23.10±21.79	36.45±29.36	11.663	0.003
Level of BMPCs					
BMPCs <15	24 (72.7%)	30 (44.1%)	9 (31.0%)	11.82	0.003
BMPCs >15	9 (27.3%)	38 (55.9%)	20 (69.0%)		
Megs					
Abundant	1 (3.0%)	2 (2.9%)	0 (0.0%)	8.941	0.538
Decreased	4 (12.1%)	13 (19.1%)	9 (31.0%)		
Increased	3 (9.1%)	3 (4.4%)	2 (6.9%)		
Normal	23 (69.7%)	45 (66.2%)	15 (51.7%)		
Partial dilution	0 (0.0%)	0 (0.0%)	1 (3.4%)		
Missed	2 (6.1%)	5 (7.4%)	2 (6.9%)		
Granulopoiesis					
Decreased	4 (12.1%)	8 (11.8%)	7 (24.1%)	3.839	0.871
Depressed	2 (6.1%)	6 (8.8%)	2 (6.9%)		
Increased	1 (3.0%)	1 (1.5%)	0 (0.0%)		
Normal	24 (72.7%)	48 (70.6%)	18 (62.1%)		
Missed	2 (6.1%)	5 (7.4%)	2 (6.9%)		

Table 5. Association between R/ISS Stage and Inflammatory Indices

Inflammatory indices	R/ISS stage			Test value	p-value
	Stage I (n=33)	Stage II (n=68)	Stage III (n=29)		
AMC					
<0.2	2 (6.1%)	0 (0.0%)	0 (0.0%)	7.345	0.29
0.2-1	29 (87.9%)	61 (89.7%)	26 (89.7%)		
1-1.25	0 (0.0%)	3 (4.4%)	1 (3.4%)		
>1.25	2 (6.1%)	4 (5.9%)	2 (6.9%)		
iPLR					
<1.95	20 (60.6%)	15 (22.1%)	14 (48.3%)	19.132	0.014
1.95 - 2.58	5 (15.2%)	13 (19.1%)	4 (13.8%)		
2.59 -3.75	5 (15.2%)	19 (27.9%)	3 (10.3%)		
3.76 -5.84	1 (3.0%)	11 (16.2%)	3 (10.3%)		
>5.84	2 (6.1%)	10 (14.7%)	5 (17.2%)		
MLR					
≤0.53	30 (90.9%)	53 (77.9%)	27 (93.1%)	4.936	0.085
>0.53	3 (9.1%)	15 (22.1%)	2 (6.9%)		
NLR					
≤2.57	27 (81.8%)	35 (51.5%)	18 (62.1%)	8.65	0.013
>2.57	6 (18.2%)	33 (48.5%)	11 (37.9%)		
PLR					
≤55	30 (90.9%)	59 (86.8%)	29 (100.0%)	4.251	0.119
>55	3 (9.1%)	9 (13.2%)	0 (0.0%)		
PNI (Mean±SD)	161.18±47.12	135.15±54.60	163.48±60.56	7.725	0.021
AAPR					
≤0.4	12 (36.4%)	44 (64.7%)	16 (55.2%)	7.223	0.027
>0.4	21 (63.6%)	24 (35.3%)	13 (44.8%)		

Table 6. Univariate and Multivariate Cox Regression Analysis for Overall Survival

Variables	Univariate			Multivariate		
	HR	95% CI	p-value	HR	95% CI	p-value
Age >60 y	1.18	0.780–1.790	0.42	1.12	0.720–1.750	0.6
R/ISS Stage II-III vs I	1.356	0.842–2.183	0.27	1.28	0.750–2.200	0.36
AMC ≥1 vs <1	1.478	0.912–2.393	0.11	1.32	0.805–2.165	0.27
iP/L ratio >2.58 vs ≤2.58	1.215	0.784–1.882	0.38	1.14	0.720–1.805	0.56
MLR >0.53 vs ≤0.53	0.958	0.553–1.659	0.89	0.925	0.520–1.645	0.79
NLR >2.57 vs ≤2.57	1.832	1.126–2.981	0.015*	1.71	1.045–2.800	0.031*
PLR >55 vs ≤55	1.037	0.578–1.859	0.912	0.995	0.550–1.800	0.988
PNI ≤150 vs >150	1.674	1.032–2.714	0.037*	1.592	0.980–2.580	0.049*
AAPR ≤0.4 vs >0.4	1.293	0.825–2.028	0.26	1.21	0.770–1.900	0.4

HR=Hazard Ratio; CI=Confidence Interval; *p-value <0.05 is significant; p-value >0.05 is insignificant

and survival, can stop megakaryocyte colony-forming units from maturing [21, 36]. Additionally, it has been noted that patients with MM have a markedly shorter platelet half-life [37, 38]. In line with a prior study on the predictive variables of NDMM, we also discovered that low NLR was associated with early disease stage [39]. In NDMM, the NLR is thought to be a marker reflecting the degree of protumorous inflammatory status, and high NLR was linked to a worse overall survival, consistent with earlier reports. The NLR directly reflects the balance between neutrophilia and lymphopenia, and elevated NLR has been identified as a poor prognostic factor in various malignancies [40, 41]. Elevated MLR was found to be associted in multiple myeloma patients with poor disease course according to several reports, however in our study we couldn't prove this association and MLR was not linked to a dismal disease course which can be attributed to small sample size, or difference in population charecteristics [5-7, 42].

Originally used to evaluate preoperative nutritional status, surgical risk, and postoperative problems in surgical patients, the PNI index is a nutritional indicator based on blood albumin and lymphocyte counts [37]. According to our research, a low PNI index was linked to a more advanced stage of the disease and a lower overall survival rate. This finding was consistent with a Chinese study that looked into how nutritional status affected the prognosis of NDMM patients [21].

Finally, we examined in our study is AAPR, which is mostly based on serum albumin and alkaline phosphatase levels, both of which are significantly impacted in MM. In line with a prior study examining the impact of nutritional and inflammatory indices on NDMM patients, we discovered that a low AAPR index was linked to a worsening of the disease and a bleak result [19].

Conclusion and recommendations

One of the most common hematologic neoplasms with a heterogeneous nature is MM. In a cohort of 132 patients, we examined seven inflammatory and nutritional markers (NLR, AMC, MLR, PLR, iPLR, PNI, and AAPR) in NDMM. Those inflammatory indices can be readily used in patients' prognostications. We found that those markers are worthy in the prediction of poor myeloma course and outcome as seen with low PLR and high iPLR, low NLR is associated with an early disease stage and hence a better outcome, while a poor outcome is observed with high NLR. Lower PNI and AAPR are associated with a poorer stage of myeloma and a lower chance of survival. An elevated NLR remained an independent predictor of worse overall survival in myeloma patients. Nutritional and inflammatory indices are simple, feasible, cost effective tests that can be routinely used to forecast the course of a disease and the prognosis in myeloma patients.

Limitations

This study has several limitations. First, the relatively small sample size (n = 130), particularly within certain subgroups such as stage III patients, may limit statistical power and the robustness of subgroup analyses. Second, multiple comparisons were performed when evaluating seven inflammatory and nutritional indices across different outcomes, which may increase the risk of type I error despite statistical precautions. In addition, the median follow-up duration of 21 months is relatively short for multiple myeloma, and longer follow-up would provide more mature survival data and stronger confirmation of long-term prognostic significance.Therefore, larger, multicenter prospective studies are warranted to validate these findings and confirm the prognostic utility of these indices in multiple myeloma.

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Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the National Cancer Institute in accordance with the Declaration of Helsinki number CP2405-303-025.

Consent for publication

Applicable.

Availability of data and materials

Data are readily available upon request from the corresponding author, but are not supported in the supplementary files.

Competing interests

The authors declare that they have no competing interests.

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