

CLINICAL STUDY

The relationship between malnutrition and neutrophil-to-lymphocyte ratio in hospitalized older patients

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ABSTRACT

OBJECTIVES: Aging is characterized by appetite loss and cachexia, i.e., factors that contribute to malnutrition. An inflammation marker, neutrophil-to-lymphocyte ratio (NLR), is a significant prognostic predictor of many geriatric syndromes. We aim to determine the association between NLR and malnutrition. **METHODS:** We designed a retrospective study on hospitalized patients in the geriatric unit of a university hospital between January 2019 and January 2021. Demographic data, chronic diseases, history of smoking, length of hospital stay, number of drugs, laboratory and further examinations, and comprehensive geriatric assessment scores were recorded from the hospital data system. The nutritional status of the patients was evaluated using the mini-nutritional assessment (MNA) questionnaire. **RESULTS:** Of the 220 patients, 121 (55 %) were female, and the mean age was 77.9 ± 7.3 years. According to the MNA, 60 % ($n = 132$) were malnourished or at risk of malnutrition. As many as 47.3 % ($n = 104$) of the patients had depressive symptoms, and 41.4 % ($n = 91$) were cognitively impaired. The mean age (79.3 ± 7.3), NLR, and GDS scores were significantly higher, and MMSE scores were significantly lower in malnourished patients or in those at risk of malnutrition as compared to patients with normal nutritional status. We showed that NLR (OR: 1.248; 95% CI: 1.066–1.461; $p = 0.006$), age (OR: 1.056; 95% CI: 1.005–1.109; $p = 0.031$), depressive symptoms (OR: 1.225; 95% CI: 1.096–1.369; $p < 0.001$), and cognitive impairment (OR: 0.829; 95% CI: 0.739–0.931; $p = 0.002$) were independently associated with malnutrition. ROC curve showed that the optimum cut-off value to predict malnutrition risk was $NLR > 4.5$, with a sensitivity of 37.9 %, specificity of 85.2 %, negative predictive value of 47.8 %, and positive predictive value of 79.4 %. **CONCLUSION:** NLR, age, depressive symptoms, and cognitive impairment were independently associated risk factors for malnutrition. NLR may be a useful nutritional marker for evaluating the nutritional status of hospitalized geriatric patients (Tab. 4, Fig. 1, Ref. 28). Text in PDF www.elis.sk

KEY WORDS: malnutrition, neutrophil-to-lymphocyte ratio, geriatric syndromes, inpatient, older adults.

Introduction

The elderly population is on the increase worldwide. Geriatric syndromes include functional impairment, cognitive impairment, malnutrition, urinary incontinence, falls, depression, and polypharmacy. They have common risk factors that affect each other.

Malnutrition is a common part of the geriatric syndrome. Older adults tend to be more prone to malnutrition, widening range of chronic diseases, cognitive and physical decline, depressed mood, poor oral health, and range of low-socioeconomic conditions and dysfunctions. All these factors can directly affect the balance between nutritional needs and ingested nutrients (1, 2). Malnutrition

has been associated with prolonged hospital stays, frequent hospital admissions, morbidity and mortality, and immune dysfunction (3).

The nutritional status of the elderly is evaluated using many screening tools. Tools such as Mini Nutritional Assessment (MNA), Nutritional Risk Screening 2002 (NRS-2002), Geriatric Nutritional Risk Index (GNRI), and Malnutrition Universal Screening Tool (MUST) can also be used (4, 5, 6). The nutritional status can be evaluated with some additional parameters. Anthropometric measurements such as weight, height, and arm-calf circumference, as well as daily diet tracking, and laboratory blood tests such as serum albumin and total cholesterol help to assess the patient's nutritional status (6).

Neutrophil-to-lymphocyte ratio (NLR) is a parameter that can be easily calculated from the complete blood count results and indicates systemic inflammation. NLR is associated with mortality, morbidity, and prognosis in many chronic diseases and malignancy (7–10). An inflammation marker, NLR, is a significant prognostic predictor for many geriatric syndromes. Studies in the literature show that inflammatory cytokines are increased in malnutrition, and malnutrition is the most common cause of immunodeficiency worldwide (11).

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Tab. 1. demographic and clinical characteristics of the patients according to the nutritional status.

Characteristics	Total patients	Normal nutrition (MNA score 24-30) (n=88)	Malnourished or at risk of malnutrition (MNA score < 24) (n=132)	P
Age (years), mean±SD	77.9±7.3	75.77±6.9	79.3±7.3	<0.001
Length of stay	22±14	22.1±14	21.9±14	0.921
Gender, n (%)				
Female	121 (55%)	44 (50.0%)	77 (58.3%)	
Male	99 (45%)	44 (50.0%)	55 (41.7%)	0.224
Smoking (pack/year), mean±SD	13±25.3	15.0±22.5	11.6±27	0.329
Number of chronic diseases	2.3±1.6	2.0±1.5	2.5±1.5	0.030
Comorbidity, n (%)				
HT	152 (69.1%)	57 (64.8%)	95 (72.0%)	0.258
DM	96 (43.6%)	34 (38.6%)	62 (47.0%)	0.222
CAD	69 (31.4%)	23 (26.1%)	46 (34.8%)	0.172
Atrial fibrillation	39 (17.7%)	13 (14.8%)	26 (19.7%)	0.349
CKD	39 (17.7%)	11 (12.5%)	28 (21.2%)	0.097
CHF	38 (17.3%)	16 (18.2%)	22 (16.7%)	0.771
Dementia	32 (14.5%)	10 (11.4%)	22 (16.7%)	0.274
COPD	25 (11.4%)	10 (11.4%)	15 (11.4%)	-
CVD	21 (9.5%)	6 (6.8%)	15 (11.4%)	0.261
Thyroid disease	18 (8.2%)	7 (8.0%)	11 (8.3%)	0.920
Rheumatological disease	15(6.8%)	5 (5.7%)	10 (7.6%)	0.585
Osteoporosis, n (%)	67 (30.5%)	24 (27.3%)	43 (32.6%)	0.402
Urinary incontinence, n(%)	13 (5.9%)	5 (5.7%)	8 (6.1%)	0.907
Number of drugs, mean±SD	5.8±3.8	5.2±3.6	6.2±3.8	0.048
Weight loss, n (%)	78 (35.5%)	16 (18.2%)	62 (47%)	<0.001
MNA score, mean±SD	21.2±2.8	26.0±2.4	18.1±2.8	<0.001
GDS, mean±SD	4.7±3.0	3.6±2.6	5.4±3.2	<0.001
MMSE score, mean±SD	23.5±3.4	25.0±3.2	22.5±3.4	<0.001

HT – hypertension; DM – diabetes mellitus; CAD – coronary artery disease; CKD – chronic kidney disease; CHF – congestive heart failure; COPD – chronic obstructive pulmonary disease; CVD – Cerebrovascular disease; MNA; Mini-Nutritional Assessment; SNAQ – Simplified Nutritional Appetite Questionnaire; GDS – Geriatric Depression Scale; MMSE – Mini-Mental State Examination. Significant p values are in bold font; p < 0.05 was considered statistically significant

In this study, we aimed to investigate the relationship and usability of NLR in assessing malnutrition and risk of malnutrition in older adults.

Materials and methods

Participants and study design

This study was designed in a retrospective manner and cross-sectional structure. A total of 315 participants were assessed for eligibility from the population aged 65 years and older who were hospitalized in the Istanbul University Cerrahpasa Medical Faculty’s inpatient clinic unit between January 01, 2019, and January 01, 2021. The data were collected from electronic medical records and patient files. Some exclusion criteria were determined for the study. Patients with a clinical diagnosis of malignancy (n = 33), and those with active infection (n = 22), terminal illness (n = 21), and missing data (n =19) were excluded from this study. After exclusion, a total of 220 participants were analyzed for this study. Sociodemographic characteristics and medical history, such as age, gender, medications, comorbidities and laboratory findings were

recorded. Unintentional weight loss was defined as a loss of 5 % of body weight in one month or 10 % over a period of six months or longer and was based on the patient’s or caregiver’s verbal statement (12). The use of 5 or more drugs per day was defined as polypharmacy (13). In addition, mini-mental state examination (MMSE) and short form of geriatric depression scale (GDS), which are parts of comprehensive geriatric assessment were examined. MMSE scale was used to determine cognitive impairment. A score below 24 (out of 30 points) on the test was accepted as a cognitive impairment (14). The possibility of depression being present was evaluated with the short form of GDS and a score of 5 or more was considered to be indicative of depressive symptoms (15).

Ethical permission was obtained from the local ethics committee for this research (Ethics Committee number: 09.09.2020-117344). This study was conducted according to the guidelines in the Declaration of Helsinki.

Assessment of nutritional status

The nutritional status of the patients was evaluated using the mini-nutritional assessment (MNA) questionnaire. MNA is composed of 18 questions aimed at anthropometric measurements (weight, height, and weight loss), global assessment (six questions related to lifestyle, medication, and mobility), dietary questionnaire (eight questions related to the number of meals, food and fluid intake, and autonomy of feeding), and subjective assessment (self-perception of health and nutrition). The MNA score was calculated as the sum of points assigned to the responses to 18 items. A score of < 24 out of the total of 30 points indicates that the patient is malnourished (MNA < 17) or at risk of malnutrition (MNA between 17 and 23.5) (16).

Statistical analysis

The data were analyzed by the Statistical Package for Social Sciences (SPSS for Windows, v21.0; IBM Corp. Armonk, NY, USA). Descriptive statistics were given as mean and standard deviations (SD) for continuous variables. Categorical variables were given as counts and percentages. The chi-square test was performed for categorical variables. Student’s t-test and ANOVA test were used to compare differences in continuous variables between the two groups because they were all normally distributed. The Mann-Whitney U-test and Kruskal-Wallis were conducted to compare the differences in continuous variables between the two groups when they did not distribute normally. A comparison of categorical variables between groups according to the nutritional status

Tab. 2. The laboratory finding of the patients according to their nutrition status.

	Normal nutrition (MNA score 24-30) (n=88)	Malnourished or at risk of malnutrition (MNA score < 24) (n = 132)	P
WBC	7116±2565	7783±2890	0.081
Hgb	11.28±1.9	10.66±1.8	0.002
MCV	85.04±9.9	83.60±8.0	0.235
MPV	8.83±1.3	8.77±1.3	0.668
Neutrophils	4.42±1.8	5.5±2.7	0.001
Lymphocytes	1.69±0.75	1.64±1.24	0.762
NLR	3.07±1.97	4.14±2.61	0.001
Platelets	247.605±120.241	275.066±140.314	0.134
Urea	46.0±22.2	51.5±25.9	0.108
Creatinine	1.0±0.42	1.11±0.59	0.172
ALT	16.24±10.34	21.28±29.3	0.123
AST	21.4±9.45	26.0±27.3	0.128
LDH	263±219	260±169	0.909
CRP	21.5±36.3	28.4±40.2	0.192
ESR	42.5±34.6	50.1±33.0	0.101
Ferritin	248.2±771	266.7±410	0.818
Vitamin B12	558±415	650±518	0.165
Folate	7.9±4.2	8.5±9.6	0.547
Albumin	3.8±0.6	3.6±0.6	0.190
Fibrinogen	346±174	365±154	0.394
D-dimer	1.70±2.2	1.85±2.3	0.656

WBC – white blood count; Hgb – hemoglobin; MCV – mean corpuscular volume; MPV – mean platelet volume; NLR – neutrophil-lymphocyte ratio; ALT – alanine aminotransferase; AST – aspartate aminotransferase; LDH – lactate dehydrogenase; CRP – C-reactive protein; ESR – erythrocyte sedimentation rate

was performed using Pearson’s χ^2 test with continuity correction or Fisher’s exact test, where appropriate. Spearman correlation analysis was performed for malnutrition, neutrophil-to-lymphocyte ratio, and associated nutritional parameters. Receiver-operating characteristic (ROC) analysis was performed to determine the importance of NLR in the diagnosis of malnutrition. We performed a multivariate logistic regression analysis of associated factors for malnutrition. A p value of < 0.05 was accepted as statistically significant. We reported multivariate associations as odds ratio (OR) with 95% confidence interval (CI).

Results

Overall, 220 elderly participants (121 females, 99 males; mean age: 77.9 ± 7.3 years) were included in the analysis. The mean length of stay in the hospital was 22 ± 14 days. The mean number of chronic diseases was 2.3 ± 1.6. The most common comorbidities were hypertension (in 69.1 %; n = 152) and diabetes mellitus (in 43.6 %; n = 96). The mean number of drugs was 5.8 ± 3.8. Osteoporosis was present in 30.5 % of patients (n = 67). Unintentional weight loss was detected in 35.5 % of patients (n = 78). The mean MNA score was 21.2 ± 2.8. As per the MNA results, 88 patients had a normal nutritional status (40 %), whereas 132 patients (60%) were malnourished (n = 35; 15.9 %) or at risk of

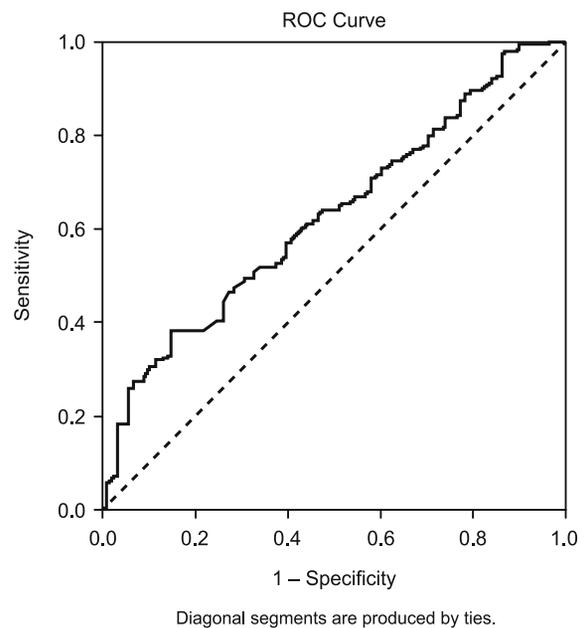


Fig. 1. ROC curves based on a univariate model showing the power of NLR to predict malnourishment or risk of malnutrition. The area under the curve was 0.624 (p = 0.002, 95% CI: 0.550–0.698). ROC, receiver-operating characteristic; NLR, neutrophil-to-lymphocyte ratio.

malnutrition (n = 97; 44.1 %). As many as 47.3 % of the patients (n = 104) had depressive symptoms, and 41.4 % of the patients (n = 91) were cognitively impaired. Polypharmacy was detected in 59.1 % of patients (n = 130).

Table 1 shows the demographic and clinical characteristics of the patients according to their nutritional status. The mean age of malnourished patients or of those at risk of malnutrition was 79.3 ± 7.3, i.e., significantly higher than that of patients with normal nutritional status (p < 0.001). The mean number of chronic diseases and drugs was significantly higher in malnourished patients and in those at risk of malnutrition (p = 0.030, 0.048, respectively). As expected, the weight loss was significantly higher in the malnourished patients and in those at risk of malnutrition (p < 0.001). Furthermore, malnourished participants or those at risk of malnutrition were more likely to be cognitively impaired and have depressive symptoms, as compared to participants with normal nutritional status (p < 0.001 for both of them).

The laboratory findings of patients are given in Table 2. Hemoglobin values were significantly lower (p = 0.002), and neutrophil values and NLR were significantly higher in malnourished patients or in those at risk of malnutrition (p < 0.001, for both of them).

In addition, the receiver-operating characteristic curve analysis was performed. We showed that the optimum NLR cut-off point for patients at risk of malnutrition was 4.5, with 37.9 % sensitivity and 85.2 % specificity (95% confidence interval (CI): 0.550–0.698; area under the curve: 0.624; p = 0.002), and the positive and negative predictive values were 79.4 % and 47.8 %, respectively (Fig. 1).

The correlation analysis between NLR and associated nutritional parameters is given in Table 3. There was a negative correla-

Tab. 3. Correlation between neutrophil-to-lymphocyte ratio and associated nutritional parameters.

	NLR	
	r	p
MNA	-0.194	0.004
Age	-0.130	0.054
Number of chronic diseases	0.055	0.413
Number of drugs	0.037	0.586
SNAQ	-0.033	0.631
GDS	0.157	0.020
MMSE	-0.109	0.107
Urea	0.005	0.936
Creatinine	-0.021	0.762
ALT	0.115	0.089
AST	0.173	0.010
LDH	0.155	0.022
CRP	0.311	<0.001
ESR	0.186	0.006
Ferritin	0.068	0.321
Vitamin B12	0.083	0.224
Folate	0.097	0.152
Albumin	-0.225	0.001
Fibrinogen	0.237	<0.001
D-dimer	0.044	0.514

MNA; Mini-Nutritional Assessment; NLR – neutrophil-lymphocyte ratio; SNAQ – Simplified Nutritional Appetite Questionnaire; GDS – Geriatric Depression Scale; MMSE – Mini-Mental State Examination; ALT – alanine aminotransferase; AST – aspartate aminotransferase; LDH – lactate dehydrogenase; CRP – C-reactive protein; ESR – erythrocyte sedimentation rate Significant p values are bolded. p < 0.05 was considered statistically significant

Tab. 4. Multivariate logistic regression analysis of risk factors for malnutrition in geriatric patients.

Variable	Odds ratio (95% CI)	p
NLR	1.248 (1.066–1.461)	0.006
Age	1.056 (1.005–1.109)	0.031
Number of drugs	1.069 (0.981–1.165)	0.129
GDS score	1.225 (1.096–1.369)	<0.001
MMSE score	0.829 (0.739–0.931)	0.002

NLR – neutrophil-lymphocyte ratio; GDS – Geriatric Depression Scale; MMSE – Mini-Mental State Examination Significant p values are in bold font; p < 0.05 was considered statistically significant

tion between NLRs and MNA scores ($r = -0.194$, $p = 0.004$). NLRs correlated with the GDS scores ($r = 0.157$, $p = 0.020$). There was a negative correlation between NLRs and serum albumin levels ($r = -0.225$, $p = 0.001$). There was a correlation between NLRs and many laboratory parameters such as aspartate aminotransferase (AST; $r = 0.173$; $p = 0.010$), lactate dehydrogenase (LDH; $r = 0.155$; $p = 0.022$), C-reactive protein (CRP; $r = 0.311$; $p < 0.001$), erythrocyte sedimentation rate (ESR; $r = 0.186$; $p = 0.006$) and fibrinogen ($r = 0.237$; $p < 0.001$).

The multivariate logistic regression analysis of risk factors for malnutrition in geriatric patients is shown in Table 4. We showed that NLR (OR: 1.248; 95% CI: 1.066–1.461; $p = 0.006$), age (OR: 1.056; 95% CI: 1.005–1.109; $p = 0.031$), depressive symptoms (OR: 1.225; 95% CI: 1.096–1.369; $p < 0.001$), and cognitive im-

pairment (OR: 0.829; 95% CI: 0.739–0.931; $p = 0.002$) were independently associated with malnutrition risk.

Discussion

The elderly are the fastest-growing part of the population worldwide. Malnutrition is a common factor in geriatric syndrome among the elderly, and as such, is a public health concern (17). Our results indicated that, based on the MNA, 60 % of elderly hospital patients were malnourished or at risk of malnutrition. Almost half of the patients had depressive symptoms and cognitive decline, while polypharmacy was found in more than half of them. A study showed that approximately one in three patients (31.7 %) presented with malnutrition on admission. In addition, malnourished patients were more likely to have a more extended hospital stay and be readmitted within 30 days (18). The estimated prevalence of malnutrition in the elderly increases to 29–61 % in hospitalized patients than in the general population (19).

In our study, malnourished patients, and those at risk of malnutrition were significantly older. Our results correlate with the literature as to the finding that the prevalence of malnutrition increases with age (20). Cognitive impairment in the elderly affects their daily functional status, which results in disability, dependence, and decreased oral intake. Depressive symptoms lead to disorders in eating behaviors, loss of appetite, and decreased feeding in the elderly. Depression, dementia, functional dependence, and multiple comorbidities have been associated with malnutrition (21). Similarly, our research found that the presence of depressive symptoms, cognitive impairment, and the mean number of comorbidities and drugs was significantly higher in malnourished patients or in those at risk of malnutrition.

Among the laboratory findings, hemoglobin, neutrophil, and NLR were statically associated with the nutritional status. The prevalence of anemia among the elderly is high, while malnutrition and risk of malnutrition increase the incidence of anemia (22). It is also well established that the systemic inflammatory response is associated with the presence of neutrophilia with a relative lymphocytopenia (23). This study demonstrated that neutrophil-to-lymphocyte ratio (NLR) was significantly higher in hospitalized geriatric malnourished patients or in those at risk of malnutrition as compared to patients with normal nutritional status. Inflammatory cytokines are known to cause cachexia, malnutrition and weight loss. The inflammation marker, NLR, is a significant prognostic predictor of the risk of malnutrition. The literature supports the finding that NLR is associated with the nutritional status of geriatric patients, and NLR can be a useful nutritional marker for evaluating the nutritional status of geriatric patients (24, 25). In our study, the risk of malnutrition in the elderly is significantly higher with NLR above the cut-off value of 4.5. Another study showed that ROC curve revealed that the optimum cut-off value for predicting malnutrition risk was $NLR > 4.2$ (26). In the literature, studies have identified that the normal NLR values in non-geriatric adult population in good health are between 0.78 and 3.53 (27).

Chronic immune activation, inflammation, recurrent infections, enteropathy, and microbiota composition changes result in malnutrition (28). As expected, NLR was correlated with malnu-

trition as well as with markers of inflammation such as CRP, ESR, LDH, AST, and fibrinogen. We also found a significant negative correlation between NLR and nutritional status indicators such as albumin.

Moreover, we performed a regression analysis. We showed that high NLR, elderly age, depressive symptoms, and cognitive impairment were independently associated with malnutrition.

This retrospective study has several limitations. Some anthropometric measurements such as calf circumference and upper arm circumference could not be obtained from the patient's files.

Conclusions

NLR, age, depressive symptoms, and cognitive impairment were independently associated risk factors for malnutrition. NLR may be a useful nutritional index for evaluating the nutritional status of hospitalized geriatric patients.

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Received January 7, 2023.
Accepted February 2, 2023.