Archives of Medical Research 55 (2024) 103003

ORIGINAL ARTICLE

Assessing Neutrophil-to-Lymphocyte Ratio as a Nutritional Indicator in Community-Dwelling Older Adults

Miguel Germán Borda,[a,b,c,d,1] Pablo Lafuente Sanchis,[d] Jonathan Patricio Baldera,[a,e] Francisco José Tarazona-Santabalbina,[f,g,h] Diego Andrés Chavarro-Carvajal,[b] Salomón Salazar-Londoño,[b] Mariia Bocharova,[i] Dag Aarsland,[a,i] and Antonio Martín-Marco[d]

[a] *Centre for Age-Related Medicine, Stavanger University Hospital. Stavanger, Norway*
[b] *Semillero de Neurociencias y Envejecimiento, Ageing Institute, Medical School, Pontificia Universidad Javeriana. Bogotá, Colombia*
[c] *Division of Clinical Geriatrics, Center for Alzheimer Research, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet. Stockholm, Sweden*
[d] *Unidad de Hospitalizacion Domiciliaria, Hospital Universitario de la Ribera, Alzira, Spain*
[e] *Escuela de Estadística de la Universidad Autónoma de Santo Domingo. Santo Domingo, República Dominicana*
[f] *Geriatric Medicine Department, Hospital Universitario de la Ribera, Alzira, Spain*
[g] *Centro de Investigación Biomédica en Red Fragilidad y Envejecimiento Saludable, Madrid, Spain*
[h] *Medical School, Universidad Católica de Valencia San Vicente Mártir, Valencia, Spain*
[i] *Department of Old Age Psychiatry, Institute of Psychiatry, Psychology, and Neuroscience, King's College London. London, UK*

Received for publication January 9, 2024; accepted April 23, 2024 (ARCMED-D-24-00026).

Background. In an aging population, there is an increasing need for easily accessible nutritional markers.

Aims. To determine whether the neutrophil-to-lymphocyte ratio (NLR) can serve as an effective nutritional indicator compared to the Mini-Nutritional Assessment Short Form (MNA-SF) or other common markers such as albumin and body mass index (BMI).

Methods. Data were obtained from the SABE study in Ecuador, which included participants aged 60 years or older. This cross-sectional study collected comprehensive data, including demographics, health-related factors, and physical assessments. Neutrophil and lymphocyte counts were measured by complete blood count. Nutritional status was assessed by MNA-SF, and BMI was calculated. Several physical tests were performed to evaluate the participants' functional status. Confounding variables such as age, sex, and comorbidities were considered.

Results. The final sample consisted of 1790 subjects (48.9% male). The overall median age was 68 years (IQR 64,76). BMI and lymphocytes were higher in females, while NLR was higher in males. MNA-SF showed a negative association with NLR. Similarly, lymphocyte count shows a positive association with MNA-SF. Physical tests, such as the Romberg test and the Five Times Sit-to-Stand test, also showed correlations with NLR and lymphocyte count, respectively.

Conclusion. The study results suggest a significant relationship between NLR and lymphocytes, and nutritional status. The correlation with albumin is stronger with NLR than with BMI. The simplicity and affordability of NLR may make it suitable for routine use in several medical fields, improving our understanding of the complex relationship between nutrition, inflammation, and overall health. © 2024 The Authors. Published by Elsevier Inc. on behalf of Instituto Mexicano del Seguro Social (IMSS). This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

Key Words: Nutritional status, Neutrophils, Lymphocytes, Body mass index, Inflammation.

Address reprint requests to: Miguel G. Borda, Centre for Age-Related Medicine (SESAM), Stavanger University Hospital, PB 8100, N-4068. Stavanger, Norway; E-mail: mmborda@gmail.com

0188-4409/$ - see front matter. Copyright © 2024 The Authors. Published by Elsevier Inc. on behalf of Instituto Mexicano del Seguro Social (IMSS). This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)
https://doi.org/10.1016/j.arcmed.2024.103003

Introduction

As the population ages and society becomes more aware of the importance of nutrition in the management of chronic diseases and their consequences, there is an urgent need for affordable, readily available, and practical methods to assess nutritional status (1,2). This is especially important when direct weight measurement is not possible.

Accessible tests that go beyond simple weight measurement are essential for healthcare professionals to prevent and detect malnutrition, make informed decisions, and improve people's health and well-being.

The neutrophil-to-lymphocyte ratio (NLR) is a simple and easy-to-interpret marker for assessing the balance between two different types of white blood cells and their relationship to inflammation. The rationale behind this division is that during periods of inflammation, the number of neutrophils tends to increase, while the number of lymphocytes may relatively decrease. This shift in the balance between these cell types is a characteristic feature of an inflammatory response. Calculating the NLR provides a single quantitative measure of the relative abundance of these two cell types in the bloodstream. This ratio simplifies complex immunological processes into a single numerical marker (3). In addition, numerous clinical studies have shown that an elevated NLR is associated with various inflammatory conditions and is predictive of poor outcomes in certain diseases. It has been used as a prognostic indicator for conditions such as sepsis, pneumonia, COVID-19, cancer, cardiovascular disease, stroke, etc. (4).

An elevated NLR indicates a shift toward a more pro-inflammatory state, while a lower NLR suggests a relatively healthier or less inflamed immune profile (5). This information may be valuable in the diagnosis and management of several medical conditions (3).

NLR is a marker primarily associated with inflammation, but it can also provide insight into a person's nutritional status. Previous research has associated it with the nutritional status of geriatric patients with a negative correlation between NLR and the Mini-Nutritional Assessment (MNA) (6).

Adequate nutrition is essential for maintaining a healthy immune system. Malnutrition, especially when it results in deficiencies of essential nutrients such as protein, vitamins, fatty acids, and minerals, can weaken the immune response. In addition, malnutrition can reduce the body's ability to mount an effective immune response, leading to chronic inflammation (2).

This study aims to evaluate the relationship between NLR and lymphocyte count with nutritional status in a representative sample of community-dwelling older adults. Our aim is to determine whether NLR can serve as an effective nutritional indicator. This will be compared to already widely used tools such as the Mini-Nutritional Assessment Short Form (MNA-SF) or other common markers such as albumin and body mass index (BMI).

Materials and Method

We conducted an analysis using data from the SABE (Salud, Bienestar y Envejecimiento) study conducted in Ecuador between June and August 2009. This cross-sectional study included 5,235 participants aged 60 years or older living in both rural and urban areas of Ecuador, excluding the Amazon and Galapagos regions. The study was carried out by the Instituto Nacional de Estadística y Censos (INEC), Department of Socio-Demographic Statistics, and was financed by the Ministry of Social and Economic Inclusion of Ecuador. Collaborators included the University of San Francisco de Quito, the aforementioned INEC, the Ministry of Public Health, and the Society of Geriatrics.

The SABE Ecuador study used an instrument derived from the international instrument developed for the original SABE study conducted in five Latin American capitals. The sampling methodology used was probabilistic, which was cluster-based (housing segments) and block-stratified, ensuring representation from 15 provinces of the continental country, divided into the Coast and Sierra regions, urban and rural areas, and Quito and Guayaquil. This comprehensive approach resulted in a total of 10,368 households surveyed, with 5,100 in the Sierra region and 5,268 in the Coast region, covering 864 sectors. Of the total sample, 85.8% of the subjects had complete data and were included in the subsequent analysis (7,8).

The survey covered a wide range of topics, including socio-demographic characteristics, cognitive status, health-related factors (cognitive and physical function, medication use, and health care services), social networks and family support, work and income history, housing conditions, physical performance, and exposure to violence and abuse (9,10). The sample selection and the final number of subjects included can be found in Supplementary Material 1.

Variables

Neutrophils and Lymphocytes

Lymphocytes and neutrophils were measured as part of a complete blood count, and their counts were obtained using automated hematology analyzers. Previous studies also examined additional hematological variables from the sample, while biochemical evaluation was completed in the second stage of the survey between April and August 2010 (11). Absolute counts were used and indicate the actual number of each white blood cell type per microliter (μL) of blood, reported as cells/μL.

The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count (5).

Nutritional Status

All participants underwent the MNA-SF. A score of 12–14 points on the MNA-SF was considered "normal nutritional status", a score of 8–11 points was considered "at risk of malnutrition", and a score of 0–7 points was considered "malnourished" (12). However, for the main analysis, the MNA-SF score was used as a continuous variable.

Body Mass Index

In SABE Ecuador, BMI was determined using anthropometric data. Body weight and height were measured with the patient wearing light indoor clothing, and BMI was calculated using the formula: BMI = weight (kg)/height (m^2). Four categories were determined: <18.5 kg/m^2 = underweight, 18.5–24.9 kg/m^2 = normal, 25–29.9 kg/m^2 = overweight, and >30 kg/m^2 = obese (13).

Other variables assessed included cognition, measured using the abbreviated version of the Mini-Mental State Examination (MMSE), which has been validated in several SABE studies (14,15). In addition, we assessed activities of daily living (ADLs), handgrip strength using a standardized hand dynamometer in kilograms, calf circumference (measured in centimeters), the Five Times Sit-to-Stand test (measured in seconds), the Romberg test (measured in seconds while standing with feet together), and the one-legged stance test (measured in seconds) (16).

Confounding Variables

Demographic factors such as age, sex, and comorbidity using an index of medical conditions calculated as the sum of the presence of self-reported conditions: diabetes mellitus, depression, chronic obstructive pulmonary disease (COPD), joint disease, osteoporosis, cancer, cerebrovascular events, visual problems, and heart disease.

Statistical Analysis

In the initial phase, a description of the included variables was conducted, estimating percentages for categorical variables and median with interquartile range (IQR) for numerical variables. A group comparison analysis was then performed to assess differences by sex for the variables included in the study, using the Pearson χ^2 test for categorical variables and the Mann-Whitney test for numerical variables. Correlation analysis using Spearman's Rho was then used to examine the relationships between selected variables, such as lymphocytes (cells/μL), NLR, BMI (kg/m^2), and MNA-SF. In addition, the non-parametric Kruskal-Wallis test for multiple mean comparisons was used to identify differences in both NLR and lymphocytes (cells/μL) across BMI categories (stratified by sex) and MNA-SF categories (non-stratified). Finally, linear models were fitted to explore the association between outcomes: MNA-SF, BMI, MMSE, instrumental activities of daily living (IADLs), handgrip strength (kg), calf circumference (cm), five-times sit-to-stand test (seconds), Romberg test (second), feet stand test (seconds), and one-legged stance test (seconds) with NLR, lymphocytes (cells/μL), and albumin (g/dL) as exposure variables. Other models were also fitted to examine the association between albumin (g/dL) with NLR, BMI, lymphocytes (cells/μL), and MNA-SF as exposure variables. Both models were adjusted for sex, age, years of schooling, and comorbidities. During model diagnosis, outlier observations were removed using Cook's distance criteria. A significance level of 0.05 was used for hypothesis testing. Statistical analyses were performed using R software version 4.2.1.

Ethics

This study received ethical approval from the Ethical and Scientific Committee of the Ageing Institute at Hospital Universitario San Ignacio and the Ethics Committee of the Pontificia Universidad Javeriana. SABE Ecuador was authorized by the authorities of the Ecuadorian Ministry of Health. All research procedures were conducted according to the ethical standards of the 1964 Declaration of Helsinki and its subsequent amendments. Measures were taken to protect the identity of the study subjects.

Results

The final sample consisted of 915 females and 875 males. The overall median age was 68 (IQR 64,76), BMI was higher in females (27.1 [IQR 24.1,30.2] vs. 25.1 [IQR 22.6,27.7], p-value <0.001), while lymphocyte count was lower in males (2321 [IQR 1844,2828] vs. 2358 [IQR 1952,2860], p-value: 0.049) and NLR was higher in males (1.53 [IQR 1.14,2.02] vs. 1.39 [IQR 1.05,1.81], p-value <0.001). (Table 1).

Mini Nutritional Assessment

The MNA-SF showed a negative association with NLR (estimate: –0.0935, SE: 0.0445, p-value: 0.0357). Similarly, lymphocyte count showed a positive association with MNA-SF (estimate: 0.00014, SE: 0.00005, p-value: 0.003). See Table 2 and Figure 1.

Regarding the physical tests, the Romberg test was correlated with NLR (estimate: 0.5337, SE: 0.2076, p-value: 0.0102); and the five-times sit-to-stand test, measured in seconds, was negatively associated with the lymphocyte count (estimate: –0.00096, SE: 0.00037, p-value: 0.010). (Table 2).

Mean Differences Using MNA-SF Cut Points are Shown in Supplementary Material 2–4.

Table 1. General characteristics of the sample

Characteristics	Females $n = 915$ (51.1%)	Males $n = 875$ (48.9%)	Overall $n = 1\,790$ (100%)	p**
Age, median (IQR)	69 (64,75)	68 (64,77)	68 (64,76)	0.978
Years of education, median (IQR)	3 (3,3)	3 (3,3)	3 (3,3)	0.958
BMI (kg/m^2), median (IQR)	27.1 (24.1,30.2)	25.1 (22.6,27.7)	26.0 (23.3,29.0)	<0.001
BMI categorize (kg/m^2), (%)[a]				
Underweight	19 (2.2%)	21 (2.5%)	40 (2.3%)	<0.001
Normal	259 (29.8%)	394 (46.5%)	653 (38.1%)	
Overweight	361 (41.6%)	341 (40.2%)	702 (40.9%)	
Obese	229 (26.4%)	92 (10.8%)	321 (18.7%)	
Lymphocytes (cells/μL), median (IQR)	2358 (1952,2860)	2321 (1844,2828)	2340 (1898,2840)	0.049
Neutrophils (cells/μL), median (IQR)	3270 (2648,4022)	3480 (2872,4308)	3380 (2755,4153)	<0.001
Neutrophil-to-lymphocyte ratio (NLR), median (IQR)	1.39 (1.05,1.81)	1.53 (1.14,2.02)	1.45 (1.09,1.90)	<0.001
Albumin (g/dL), median (IQR)	4.36 (4.19,4.55)	4.38 (4.18,4.57)	4.37 (4.18,4.56)	0.431
Mini Nutritional Assessment Short Form (MNA-SF), median (IQR)	12 (11,13)	12 (11,13)	12 (11,13)	0.817
Mini Nutritional Assessment Short Form (MNA-SF) Categorize, (%)*				
Normal nutritional status	606 (71.7%)	580 (70.9%)	1186 (71.3%)	0.289
At risk of malnutrition	236 (27.9%)	230 (28.1%)	466 (28.0%)	
Malnourished	3 (0.4%)	8 (1.0%)	11 (0.7%)	
Mini Mental State Examination (MMSE), median (IQR)	16 (13,18)	16 (14,18)	16 (14,18)	0.014
Instrumental Activity of Daily Living (IADLs), median (IQR)	7 (3.75,17)	6 (3,16.5)	7 (3,17)	0.569
Handgrip strength (kg), median (IQR)	18 (14,22)	29 (24,34)	22 (18,30)	<0.001
Calf circumference (cm), median (IQR)	34.3 (32,37)	34.7 (32.4,37)	34.5 (32.2,37)	0.050
Number of comorbidities, median (IQR)	2 (1,3)	1 (0,2)	1 (0,3)	<0.001
Five Times Sit-to-Stand test (seconds), median (IQR)	12 (10,15)	11 (9,13)	12 (10,15)	<0.001
Romberg test, stands with feet together (seconds), median (IQR)	10 (10,10)	10 (10,10)	10 (10,10)	0.818
One-legged stance test (seconds), median (IQR)	10 (10,10)	10 (10,10)	10 (10,10)	0.572

*Missing was excluded
**Differences between groups (sex).

Table 2. Estimated values for Neutrophil-to-lymphocyte ratio (NLR) and Lymphocytes

Dependent variable*	Neutrophil-to-lymphocyte ratio (NLR)			Lymphocytes (cells/μL)		
	Estimate	Standard error	p	Estimate	Standarderror	p
Mini Nutritional Assessment Short Form (MNA-SF)	-0.0935	0.0445	0.035	0.00014	0.00005	0.003
BMI (kg/m^2)	-0.0409	0.1233	0.740	0.00057	0.00014	<0.001
Mini Mental State Examination (MMSE)	0.1169	0.0790	0.139	-0.00012	0.00009	0.171
Instrumental Activity of Daily Living (IADLs)	-0.3977	0.6102	0.515	0.00115	0.00063	0.067
Handgrip strength (kg)	-0.2820	0.1878	0.133	-0.00019	0.00021	0.358
Calf circumference (cm)	-0.1130	2.5143	0.964	0.00401	0.00277	0.148
Five Times Sit-to-Stand test (seconds)	0.3535	0.3776	0.349	-0.00096	0.00037	0.010
Romberg test, stands with feet together (seconds)	0.5337	0.2076	0.010	-0.00041	0.00021	0.055
One-legged stance test (seconds)	1.0973	0.6673	0.100	-0.00049	0.00074	0.507

*Adjusted for sex, age, years of schooling, and comorbidities.

Albumin

Albumin showed a significant negative association with NLR, with an estimated coefficient of –0.03447 and a SE of 0.00883 (p <0.001). However, when examining albumin with BMI, we found no significant association (estimated coefficient: 0.00024, SE 0.00173, $p = 0.890$). Lymphocyte count (cells/μL) demonstrated a positive association with albumin, with an estimated coefficient of 0.00002, an SE of 0.00001, and a p-value of 0.048. However, the MNA-SF showed no significant association (estimated coefficient: 0.00985, SE 0.00512, $p = 0.054$). Table 3, Figure 2.

Discussion

This study demonstrated a significant relationship between the nutritional status as measured by MNA-SF and NLR. The MNA-SF showed a negative association with the NLR, indicating a relationship between nutritional status, as mea-

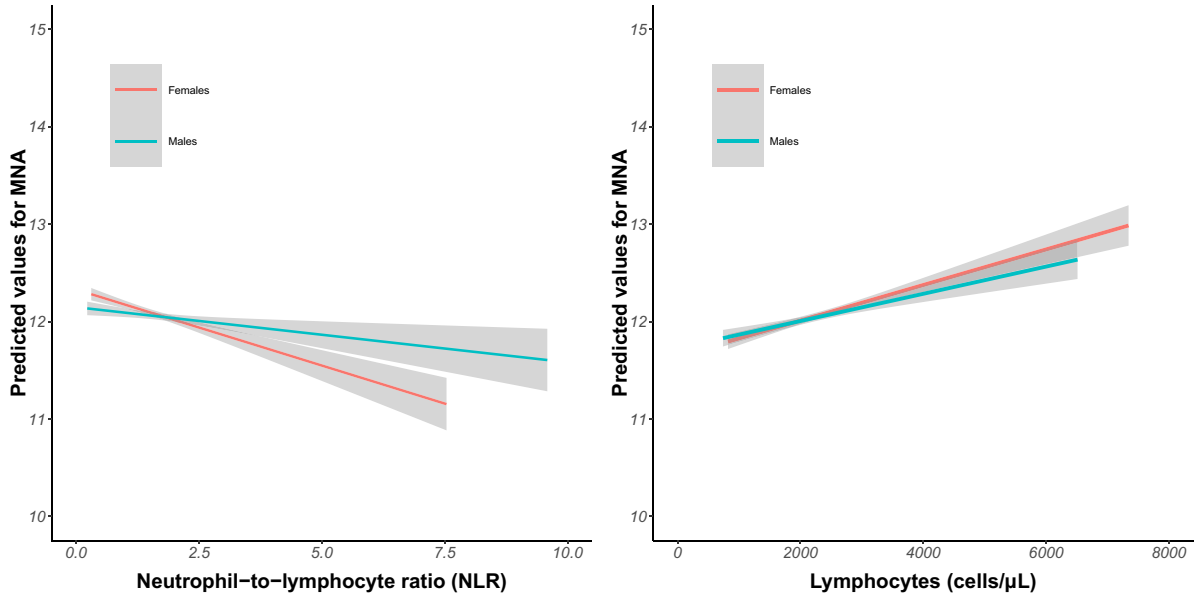


Figure 1. Linear adjusted association between NLR and lymphocytes with MNA.

Table 3. Association between NLR, BMI, lymphocytes and MNA with albumin

Exposure variable*	**Albumin (g/dL) as a dependent variable**		
	Estimate	**Standard error**	***p***
Neutrophil-to-lymphocyte ratio (NLR)	-0.03447	0.00883	<0.001
BMI (kg/m^2)	0.00024	0.00173	0.890
Lymphocytes (cells/μL)	0.00002	0.00001	0.048
Mini Nutritional Assessment Short Form (MNA-SF)	0.00985	0.00512	0.054

*Adjusted for sex, age, years of schooling, and comorbidities

sured by this widely validated and used tool, and white blood cell distribution, as calculated by the NLR. Similarly, lymphocyte count itself showed a positive association with MNA-SF. These findings provide valuable insights into the relationships between traditional clinical variables for detecting malnutrition with simple blood count tests such as NLR and lymphocyte count. Our results highlight the potential usefulness of NLR in the context of determining physical health and its potential utility as a tool to determine malnutrition in aging.

In clinical practice, there is an ongoing dilemma regarding the accuracy of anthropometric measurements originally designed to assess younger individuals. This is particularly evident in the case of BMI, waist circumference, or calf circumference. If the distribution between muscle mass and body fat cannot be accurately differentiated, conditions such as sarcopenic obesity are overlooked. Additionally, when treating older adults, it is common to encounter difficulties in measuring height and weight due to pain, bedridden conditions, or acute illnesses. NLR provides the opportunity to estimate nutritional status using commonly available blood tests.

Previous studies in different contexts have provided support for our findings. First, a study by Luqiong Liu and colleagues examined the relationship between heart failure and markers of malnutrition, inflammation, and thyroid function, specifically, the Geriatric Nutritional Risk Index (GNRI), NLR, and free triiodothyronine (FT3). This study included 454 elderly patients with heart failure, and found that low GNRI and FT3, along with high NLR, were associated with an increased risk of major adverse cardiovascular events (MACEs). Moreover, low FT3 emerged as an independent predictor of MACEs, and the combination of GNRI, NLR, and FT3 significantly improved the predictability of adverse events, emphasizing the importance of these markers in assessing clinical prognosis (17).

A related investigation focused on the relationship between malnutrition and the NLR in hospitalized elderly patients. This retrospective study included 220 patients and showed that 60% of them were malnourished or at risk of malnutrition according to MNA. The study highlighted significant associations between NLR, age, depressive symptoms, cognitive impairment, and malnutrition. Notably, NLR emerged as an independent risk factor for

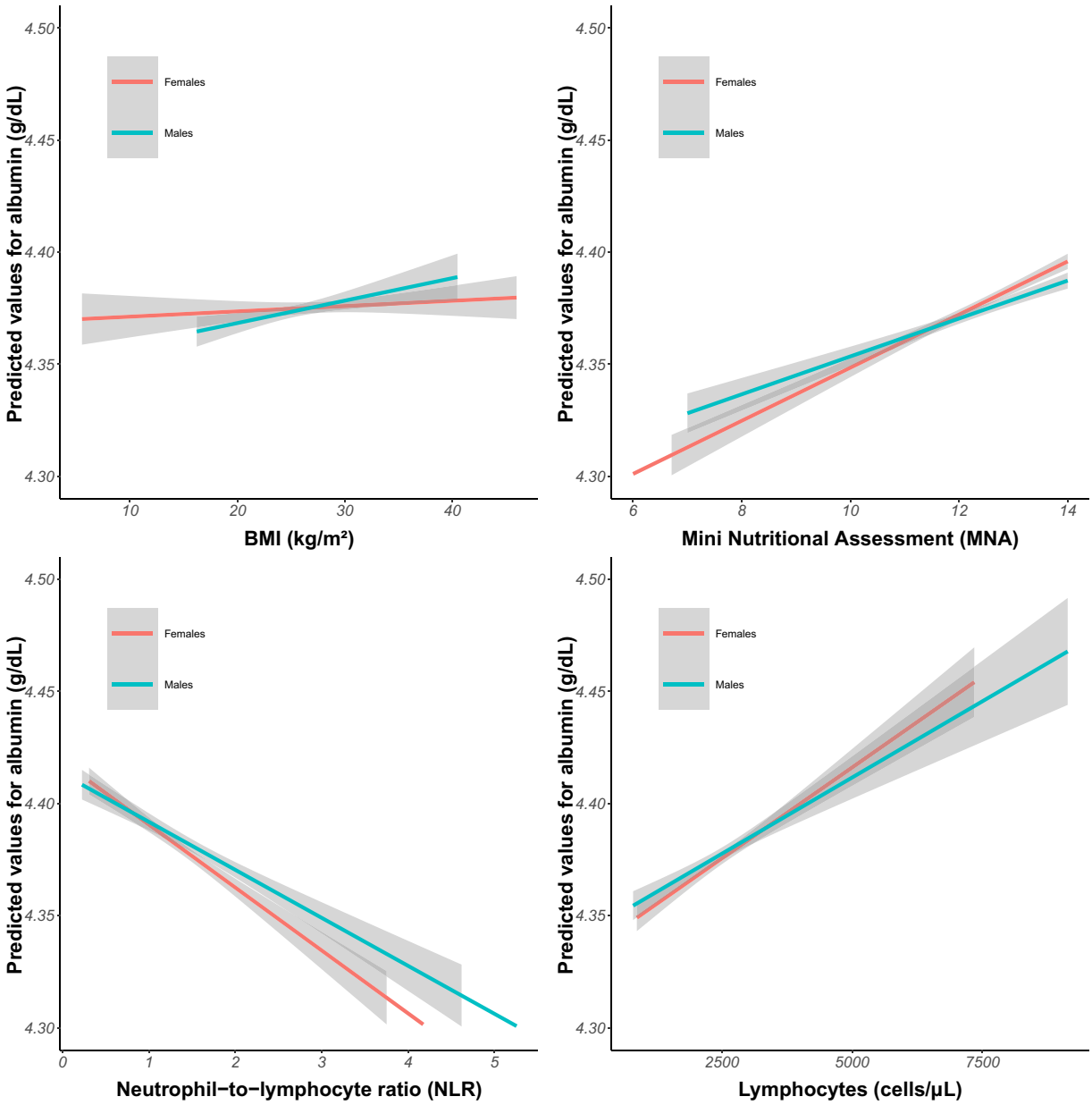


Figure 2. Association between albumin with BMI, MNA, NLR, and lymphocytes.

malnutrition, with an optimal cutoff point of NLR >4.5 to predict malnutrition risk. This study highlights the utility of NLR as a valuable nutritional marker for assessing the nutritional status of hospitalized geriatric patients (18).

Finally, Tezcan Kaya and colleagues explored the association between NLR and nutritional status in geriatric patients through a cross-sectional study involving 95 patients (6). Their analysis revealed that 48.4% of patients were malnourished or at risk of malnutrition, and NLR was significantly higher in this group compared to patients with normal nutritional status. Furthermore, there was a negative correlation between NLR and MNA scores, meaning that elevated NLR was independently predictive of malnutrition or the risk of malnutrition in geriatric patients. This study provides further evidence for the relevance of NLR as a nutritional marker, particularly in the context of geriatric outpatient care.

In addition, recent research has increasingly focused on NLR as a potential biomarker for several mental disorders in geriatric populations. A meta-analysis by Cheng Y, et al. corroborated elevated NLR levels in patients with major depression, with a pronounced effect in individuals with post-stroke depression (19). Moreover, at least two

studies have shown that NLR is elevated in late-life depression (20,21), confirming potential inflammatory mechanisms behind this condition – as highlighted by a wealth of research on cytokines and chemokines (22,23). Furthermore, a prospective study by Ramos-Cejudo J, et al. identified NLR as a potential predictor of dementia onset, along with factors such as age, history of cardiovascular disease, and baseline blood pressure (24). These findings underscore the critical need for further investigation of NLR as a marker of malnutrition, as well as a biomarker in aging and geriatric conditions.

The rationale behind the association between variations in white blood cell counts and nutritional status is rooted in our understanding of how the body responds to systemic inflammation (4). When the body encounters a state of inflammation, whether due to infection, disease, or other factors, it triggers a series of immune responses. A key aspect of this response is the modulation of different types of white blood cells, including lymphocytes and neutrophils (3). Inflammation is a catabolic state and therefore has the potential to decrease nutritional reserves and increase body wasting (25).

We also included BMI as a nutritional variable in our assessment. There was a significant correlation between BMI and lymphocyte count, with lower BMI values associated with reduced lymphocyte count. It should be noted, however, that this correlation did not hold for NLR. The unreliability of BMI as a measure of nutrition in older adults is a well-documented phenomenon, primarily due to the significant changes that occur with aging. Importantly, BMI reflects not only fat tissue but also muscle mass. Consequently, a high BMI may indicate increased adipose tissue but may not accurately reflect increased muscle mass or overall nutritional well-being. This nuance is particularly relevant in the context of older adults, who may experience changes in body composition, including muscle loss, and have clinically relevant conditions such as sarcopenia. The same trend is evident in bone density; several studies have shown that individuals with higher BMI tend to have higher bone mass density (26). However, the presence of more obese subjects represents a population at higher risk for fractures (27). Such individuals may have a high BMI, reflecting excess fat tissue, but still have or be at risk of sarcopenia, osteoporosis, or malnutrition (28). In addition, in Supplementary Material 3, we can show how the trend of the data regarding NLR, especially in females, shows a U shape, with the best condition being overweight, but worsening with obesity.

This phenomenon was reinforced when we compared the different nutritional assessment methods in this study with albumin. BMI did not show any significant association or linear tendency and can be seen graphically in Figure 2. It should be emphasized that NLR had a strong independent association with albumin. This again confirms the usefulness of this ratio.

As for differences in hematological parameters between males and females, evidence is scarce since several studies present differences related to the evaluated outcome (e.g., fragile vs. no fragile; malnourished vs. normal nutritional status). However, it has been stated that these differences may be due to menopause, and obstetric and gynecologic history, as women, especially after menopause, tend to have a lower NLR and higher lymphocyte count, which is consistent with our data as we are dealing with older adults. This is also due to differences in cardiovascular disease between sexes, and due to the high variability of NLR in women throughout their lives, its predictive value as a cardiovascular disease risk marker may be less efficient (29). Therefore, it is important to include sex-specific analysis in the assessment of nutritional status.

Regarding the physical tests, the Romberg test yielded an interesting finding where NLR was associated with better balance and stability, and a better Five Times Sit to Stand test was associated with a higher lymphocyte count. These two associations potentially offer valuable insights into the physical well-being, mobility, and physical frailty of individuals, the latter two of which have previously been associated with increased inflammation and malnutrition (30). Moreover, NLR has the potential to be tested as a surrogate for common and disabling conditions such as sarcopenia and frailty. For the former, higher NLR has been associated with higher SARC-F scores and lower muscle performance and strength in hospitalized cancer patients (31). For the second, longitudinal analysis supports the association between higher NLR and increased odds of frailty in community-dwelling older adults (32). NLR may also provide insight into an accelerated immunosenescence process and thus help identify individuals at higher risk of morbidity, infections, and other age-related health issues (4,33).

Further studies are needed to understand whether NLR could be widely used and validated in several other contexts, perhaps to indicate nutritional deficit status, and nutritional risk, or to assess the effectiveness of nutritional interventions. In cases where malnutrition contributes to inflammation, improving nutritional status through dietary changes or supplements may lead to a reduction in NLR as the inflammation subsides (34).

NLR has become a widely used marker in various medical fields due to its accessibility and reliability in measuring the immune response to both infectious and non-infectious triggers. Previous studies have suggested a normal range of NLR between 1–2, with values above 3.0 and below 0.7 being pathological in adults. NLR in a gray zone between 2.3–3.0 may serve as an early warning of pathological conditions or processes such as cancer, atherosclerosis, infection, inflammation, psychiatric disor-

ders, and stress (3). However, as this is a new population, and to achieve better statistical accuracy, we used NLR as a continuous variable.

Although the study we used was conducted in 2009, its findings are still relevant for several compelling reasons, such as a representative sample, extensive and comprehensive data collection, and exploration of NLR as a nutritional marker, making it a valuable contribution to the understanding of the intricate relationship between nutrition, inflammation, and overall health.

This study has several limitations. First, this is a cross-sectional study; therefore, causality could not be determined. Second, this study is based on self-reported variables of comorbidity which allows for recall bias. Third, we performed a secondary analysis, which means that the variables were not collected for the specific purpose of this paper. Fourth, as noted above, BMI is a widely used tool, and it is useful for important health-related outcomes that are more likely to occur when a person is underweight or obese. However, as with most measures of health, BMI is not a perfect measure, especially in older adults, mainly because of age-related changes in the musculoskeletal system (13,35,36). Our results are also consistent with preliminary research and provide relevant information for healthcare providers and future strategies to prevent poor quality of life and disability (6). The initial sample of 5,235 was eventually reduced to 1,790 participants due to the availability of physical and blood measurements. Nevertheless, this remains a substantial and distinctive sample that effectively represents one of the largest countries in Latin America (10). Finally, future studies using the NLR should conduct more comprehensive analyses that include variables that encompass dietary, physical, and psychological aspects. These factors are captured by the MNA but are not addressed by the NLR or lymphocyte count alone.

We highlight the NLR as a potentially cost-effective measure of nutritional status. While NLR is primarily recognized as an indicator of inflammation, it is closely intertwined with nutrition, especially in the context of older adults, chronic disease, and malnutrition. Monitoring NLR in conjunction with other nutritional markers may help healthcare professionals better understand the complex relationship between nutrition, inflammation, and overall health.

Conclusion

A significant relationship was found between NLR, lymphocyte count, and nutritional status. In correlation models with albumin concentration, NLR had a stronger relationship than BMI. This work enhances our understanding of inflammation as a marker of nutrition and overall health, with NLR as a simple, affordable, and suitable routine marker that can be used in various settings.

Funding

This paper represents independent research supported by the Norwegian government, through the hospital owner Helse Vest (Western Norway Regional Health Authority) and also funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College, London.

Conflicts of Interest

The authors declare that they have no competing interests.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.arcmed.2024.103003.

References

1. Lee R. The outlook for population growth. Science 2011;333:569–573.
2. Norman K, Haß U, Pirlich M. Malnutrition in Older Adults-Recent Advances and Remaining Challenges. Nutrients 2021;13(8).
3. Zahorec R. Neutrophil-to-lymphocyte ratio, past, present, and future perspectives. Bratisl Lek Listy 2021;122:474–488.
4. Buonacera A, Stancanelli B, Colaci M, et al. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. Int J Mol Sci 2022;23(7).
5. Faria SS, Fernandes PC Jr, Silva MJ, et al. The neutrophil-to-lymphocyte ratio: a narrative review. Ecancermedicalscience 2016;10:702.
6. Kaya T, Açıkgöz SB, Yıldırım M, et al. Association between neutrophil-to-lymphocyte ratio and nutritional status in geriatric patients. J Clin Lab Anal 2019;33:e22636.
7. SENPLADES E. Encuesta de Salud, Bienestar y Envejecimiento. 2009.
8. Amano T, Gallegos CA, Waters WF, et al. Ethnic Disparities in Nutritional Status among Older Adults: Evidence from the Survey of Health, Welfare and Aging (SABE) Ecuador. J Gerontol Soc Work 2021;64:106–119.
9. Borda MG, Castellanos-Perilla N, Patiño JA, et al. Edentulism and its relationship with self-rated health: secondary analysis of the SABE Ecuador 2009 Study. Acta Odontol Latinoam 2017;30:83–89.
10. Vinueza Veloz AF, Carpio Arias TV, Vargas Mejía JS, et al. Cognitive function and vitamin B12 and D among community-dwelling elders: A cross-sectional study. Clin Nutr ESPEN 2022;50:270–276.
11. Orces CH. Vitamin D Status among Older Adults Residing in the Littoral and Andes Mountains in Ecuador. ScientificWorldJournal 2015;2015:545297.
12. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition 1999;15:116–122.
13. Borda MG, Jaramillo-Jimenez A, Giil LM, et al. Body mass index trajectories and associations with cognitive decline in people with Lewy body dementia and Alzheimer's disease. Health Sci Rep 2022;5:e590.
14. Garcia-Cifuentes E, David-Pardo DG, Borda MG, et al. TWO-WAY Bridge between Muscular Dysfunction and Cognitive Impairment: Secondary Analyses of SABE - Bogota Study. J Frailty Aging 2017;6:141–143.

15. Borda MG, Ruíz de Sánchez C, Gutiérrez S, et al. Relación entre deterioro cognoscitivo y actividades instrumentales de la vida diaria: Estudio SABE-Bogotá, Colombia. Acta Neurológica Colombiana 2016;32:27–34.
16. Patrizio E, Calvani R, Marzetti E, et al. Physical Functional Assessment in Older Adults. J Frailty Aging 2021;10:141–149.
17. Liu L, Chen Y, Xie J. Association of GNRI, NLR, and FT3 with the Clinical Prognosis of Older Patients with Heart Failure. Int Heart J 2022;63:1048–1054.
18. Avci GU, Kanat BB, Can G, et al. The relationship between malnutrition and neutrophil-to-lymphocyte ratio in hospitalized older patient. Bratisl Lek Listy 2023;124:498–502.
19. Cheng Y, Wang Y, Wang X, et al. Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Monocyte-to-Lymphocyte Ratio in Depression: An Updated Systematic Review and Meta-Analysis. Front Psychiatry 2022;13:893097.
20. Ozdin S, Sukriye BO. Does late and early onset depression differ in terms of inflammation? Dusunen Adam 2020;33:334–339.
21. Liang M, Du B, Zhang H, et al. NLR Is Associated With Geriatric Depression in Chinese Women: A Community-Based Cross-Sectional Study in Eastern China. Front Psychol 2019;10:2941.
22. Martínez-Cengotitabengoa M, Carrascón L, O'Brien JT, et al. Peripheral Inflammatory Parameters in Late-Life Depression: A Systematic Review Int. J Mol Sci 2016;17(12).
23. Ng A, Tam WW, Zhang MW, et al. IL-1β, IL-6, TNF- α and CRP in Elderly Patients with Depression or Alzheimer's disease: Systematic Review and Meta-Analysis. Sci Rep 2018;8:12050.
24. Ramos-Cejudo J, Johnson AD, Beiser A, et al. The Neutrophil to Lymphocyte Ratio Is Associated With the Risk of Subsequent Dementia in the Framingham Heart Study. Front Aging Neurosci 2021;13:773984.
25. Bano G, Trevisan C, Carraro S, et al. Inflammation and sarcopenia: A systematic review and meta-analysis. Maturitas 2017;96:10–15.
26. Lloyd JT, Alley DE, Hawkes WG, et al. Body mass index is positively associated with bone mineral density in US older adults. Arch Osteoporos 2014;9:175.
27. Rexhepi S, Bahtiri E, Rexhepi M, et al. Association of Body Weight and Body Mass Index with Bone Mineral Density in Women and Men from Kosovo. Mater Sociomed 2015;27:259–262.
28. Ponti F, Santoro A, Mercatelli D, et al. Aging and Imaging Assessment of Body Composition: From Fat to Facts. Front Endocrinol (Lausanne) 2019;10:861.
29. Trtica Majnarić L, Guljaš S, Bosnić Z, et al. Neutrophil-to-Lymphocyte Ratio as a Cardiovascular Risk Marker May Be Less Efficient in Women Than in Men. Biomolecules 2021;11(4).
30. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. J Am Med Dir Assoc 2013;14:392–397.
31. Borges TC, Gomes TL, Pichard C, et al. High neutrophil to lymphocytes ratio is associated with sarcopenia risk in hospitalized cancer patients. Clin Nutr 2021;40:202–206.
32. Xu W, Liang Y, Lin Z. Association Between Neutrophil-Lymphocyte Ratio and Frailty: The Chinese Longitudinal Healthy Longevity Survey. Front Med (Lausanne) 2021;8:783077.
33. Aiello A, Farzaneh F, Candore G, et al. Immunosenescence and Its Hallmarks: How to Oppose Aging Strategically? A Review of Potential Options for Therapeutic Intervention. Front Immunol 2019;10:2247.
34. Stumpf F, Keller B, Gressies C, et al. Inflammation and Nutrition: Friend or Foe? Nutrients 2023;15(5).
35. Babiarczyk B, Turbiarz A. Body Mass Index in elderly people - do the reference ranges matter? Progress in Health Sciences 2012;2:58–67.
36. Kim S, Leng XI, Kritchevsky SB. Body Composition and Physical Function in Older Adults with Various Comorbidities. Innov Aging 2017;1 igx008.