ORIGINAL RESEARCH

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Might the haemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score Be Associated with Prefrailty and Frailty in Older Adults without Cancer: A Cross-Sectional Study?

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Abstract

Objective: Frailty is related to both malnutrition and systemic inflammation. The aim of this study was to explore the relationship between the haemoglobin, albumin, lymphocyte, and platelet (HALP) score and different stages of frailty in community-dwelling older adults.

Materials and Methods: A total of 439 patients admitted to our geriatric outpatient clinic from January 2023 to June 2024 were included in the analysis. All participants underwent a comprehensive geriatric assessment, and frailty status was determined according to the Fried frailty phenotype. Patients were then categorized into three groups—frail, prefrail, and robust. The HALP score was calculated for each participant and compared across these three groups.

Results: The mean age of the study population was 76.12 ± 6.74 years; 71.3% were female. The frail group had a higher mean age, a higher proportion of females, and higher frequencies of dementia, recurrent falls, geriatric depression, polypharmacy, malnutrition, and probable sarcopenia compared with the prefrail and robust groups ($p < 0.05$). The median HALP score was significantly lower in the frail and prefrail groups than in the robust group (frail: 34.9 vs. 48.3, $p < 0.001$; prefrail: 38.6 vs. 48.3, $p = 0.005$). In the logistic regression analysis, after adjustment for potential confounding factors, the association remained statistically significant in both the frail and prefrail groups, compared with the robust group ($p < 0.05$).

Conclusion: The HALP score is associated with both prefrailty and frailty and may serve as a risk-stratification marker in older adults.

Keywords: Aging, frailty, geriatric syndrome, inflammation, nutrition

Introduction

Frailty is an important geriatric syndrome. Its frequency increases with age, increasing older individuals' vulnerability to stressors due to age-associated declines in function and reserve across multiple physiological systems (1,2). Frailty is associated with adverse outcomes, including disability, recurrent falls, prolonged hospital stays, and mortality in older adults (2). It has also been reported that frail individuals have lower incomes and more comorbidities than non-frail older adults (3). In this respect, screening for frailty is important in geriatric practice, and several assessment tools are available for this purpose. Of these, the most commonly used is the Fried frailty scale. According to the Fried frailty phenotype, frailty is a clinical syndrome identified when three or more of the following criteria are present: unintentional weight loss, diminished grip strength, exhaustion, decreased walking speed, and reduced physical activity (4). Patients meeting one or two of these criteria are classified as prefrail. In the literature, the frail and Fried scales are among the most commonly used tools for frailty screening, and several scoring systems have been developed to predict frailty in accordance with these scales (5). The pathophysiology of frailty is complex, involving multiple organ systems. Changes in the immune system and inflammation are frequently emphasised in its pathophysiology (1). In addition to inflammation, the pathophysiology of frailty involves mitochondrial dysfunction, dysregulated nutrient sensing, cellular senescence, oxidative

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stress, and neuroendocrine imbalance (6). Chronic inflammation may lead to frailty by increasing growth factor inhibition and catabolism in response to non-infectious triggers (6). Malnourishment is closely associated with frailty (7). From a mechanistic perspective, frailty is a multidimensional geriatric syndrome driven by chronic inflammation, immune dysfunction, and malnutrition, all of which contribute to reduced physiological reserve and increased vulnerability to stressors. Haemoglobin reflects tissue oxygenation and chronic inflammatory burden; anaemia has been consistently associated with decreased physical performance and frailty in older adults (8). Serum albumin is a marker of protein-energy status and systemic inflammation, and low albumin levels indicate catabolic states that promote muscle loss and functional decline (9). Lymphocyte count reflects immune competence, and age-related immunosenescence, characterized by lymphopenia, has been linked to increased severity of frailty (10). Platelets are active participants in inflammatory and oxidative pathways; altered platelet activation has been implicated in endothelial dysfunction and adverse outcomes commonly observed in frail individuals (11). Thus, the haemoglobin, albumin, lymphocyte, and platelet (HALP) score integrates haematologic, nutritional, and immunological components, capturing key biological pathways underlying frailty.

The HALP score serves as a straightforward and clinically relevant biomarker integrating indicators of nutritional status and inflammation (12). It has emerged as a novel biomarker for predicting adverse clinical outcomes across a range of diseases. It has also been suggested to be associated with certain malignancies and with cardiovascular mortality (12). However, there is currently no evidence in the literature examining the relationship between the HALP score and frailty.

Inflammatory markers may be helpful in predicting frailty (13). No study in the literature has shown that the HALP score, an inflammatory marker, predicts frailty. This retrospective study aimed to determine whether an association exists between the HALP score and frailty status. We hypothesized that lower HALP scores would be associated with more advanced frailty stages in community-dwelling older adults.

Materials and Methods

Study Design

This retrospective, cross-sectional study included 439 older adults who were evaluated at the geriatric outpatient clinic of Balıkesir University Hospital between January 2023 and June 2024. A Comprehensive Geriatric Assessment (CGA), including a frailty assessment, was performed for all participants. The patient selection process and reasons for exclusion are summarized in the study flow diagram (Figure 1).

Inclusion Criteria

Patients aged >65 years who had previously undergone a CGA as part of routine clinical care and who did not meet the exclusion criteria were retrospectively identified and included in this cross-sectional study.

Exclusion Criteria

The exclusion criteria included: severe anemia (haemoglobin level <7 g/dL); critical valvular heart disease; acute or chronic kidney failure (stage 4 or 5); advanced cardiac or hepatic failure, or both; malignancy; severe coronary or peripheral artery stenosis; acute exacerbations of rheumatologic or connective tissue diseases; clinically active infection; a history of cerebrovascular disease, myocardial infarction, or lower extremity fracture within the past month; evidence of acute dehydration; electrolyte imbalances such as hyponatremia, hypernatremia, or hypercalcemia; acute hemorrhage; immobility due to severe osteoarthritis or neuromuscular disease; and acute changes in mental status (7). In addition, patients with moderate to severe cognitive impairment (Clinical Dementia Rating Score ≥2), advanced Parkinson's disease (Hoehn and Yahr stage ≥2), and those with essential tremor associated with impaired activities of daily living were excluded from the study, as these conditions could compromise compliance with, and the reliability of, handgrip strength and gait speed assessments. Participants receiving iron supplementation (IV or oral), steroid use, or both were also excluded.

Patient Characteristic

Age, sex, education level, and comorbidities were evaluated. Geriatric syndromes such as polypharmacy (>5 medications), dementia, probable sarcopenia, geriatric depression, urinary

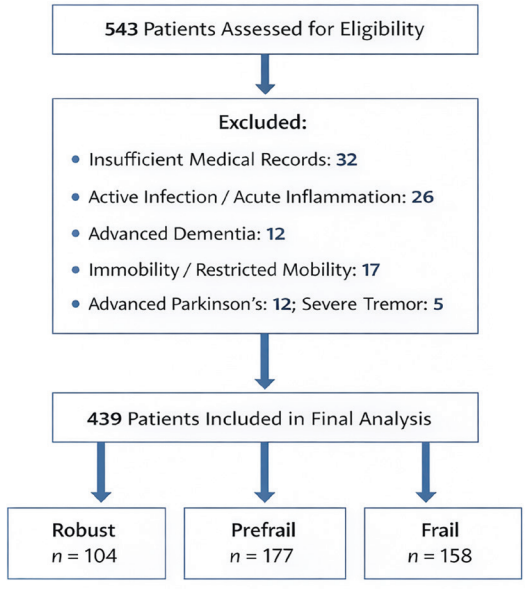

Figure 1. Flowchart of the study population and frailty categorization.

incontinence, recurrent falls within the past year, essential tremor, and malnutrition were also assessed using patients' medical records. Diagnoses of major neurocognitive disorder or dementia were established according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria (14). Probable sarcopenia was determined according to the European Working Group on Sarcopenia in Older People 2 criteria (15). Nutritional status was assessed via the mini nutritional assessment–short form (16), categorizing participants as malnourished or at risk (0–11 points) or well-nourished (12–14 points). A CGA was performed in all participants and included the Yesavage Geriatric Depression Scale, the Tinetti Performance-Oriented Mobility Assessment, the Timed Up-and-Go Test, and evaluations of basic and instrumental activities of daily living (BADL and IADL) (17–21).

Laboratory Findings

Patients' blood samples were routinely collected in the fasting state at 08:00. The haemoglobin level, platelet count, lymphocyte count, glucose level, albumin level, estimated glomerular filtration rate (eGFR), and the levels of vitamin D, folate, ferritin, thyroid-stimulating hormone, and vitamin B12 were obtained from the patients' laboratory records. All these biochemical tests were performed on Diagnostic Modular Systems auto-analysers (Roche E170 and P-800). Serum 25-hydroxyvitamin D was measured by radioimmunoassay (7). Laboratory measurements and CGA were performed on the same day.

HALP Score

The HALP score was calculated using the following formula: [haemoglobin (g/L) × albumin (g/L) × lymphocytes (/L))/platelets (/L)] (22).

Frailty Phenotype

Frailty was evaluated using Fried's physical frailty scale (4). This scale comprises five components: weakness, slowness, low physical activity, exhaustion, and unintentional weight loss (3). Based on their frailty scores, patients were categorized into three groups: robust (0 points), prefrail (1–2 points), and frail (3–5 points).

Statistics

Categorical variables were presented as percentages (%) and continuous variables as mean ± standard deviation. The patients were divided into three groups according to their frailty status: robust, prefrail, and frail. For each of the three categories, continuous and categorical variables were compared between the two dichotomous groups. In categorical variables', the chi-square test was performed for comparison between these groups. Continuous variables were first evaluated for normality using the Kolmogorov–Smirnov test, and homoscedasticity was assessed. Because not all continuous variables were normally distributed, the Mann–Whitney U test, a non-parametric test, was used to compare two groups; these variables are presented accordingly. The Kruskal-Walli's test was performed to compare the three groups. Binary logistic regression was used to assess the association of the prefrail and frail groups with the robust group. Model 0 was unadjusted for contributing factors. Model 1 was adjusted for demographic featrues including age and gender. Model 2 was adjusted for the covariates included in Model 1, plus comorbidities and geriatric syndromes. Odds ratios (ORs) were calculated with 95% confidence intervals (CIs). A p-value of <0.05 was considered statistically significant. All statistical analyses were conducted using IBM SPSS Statistics (version 22.0; Armonk, NY: IBM Corp.).

Ethical Issues

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Balıkesir University (approval number: 2024/10/01, decision number: 2024/208, dated: 03.12.2024).

Results

A total of 439 older adults (mean age 76.12 ± 6.74 years; 71.3% female) were included. The frail group was older and had a higher proportion of females compared with the prefrail and robust groups, whereas no demographic differences were observed between the prefrail and robust groups ($p > 0.05$). Parkinson's disease, geriatric depression, dementia, recurrent falls, probable sarcopenia, polypharmacy, malnutrition, and essential tremor were more common among frail individuals ($p < 0.05$). The prefrail group also showed higher frequencies of essential tremor, depression, malnutrition, and probable sarcopenia than the robust group ($p < 0.05$). Haemoglobin, albumin, and eGFR levels were significantly lower in the frail group ($p < 0.05$). Functional and mobility scores were lower in both the frail and prefrail groups than in the robust group ($p < 0.05$; Table 1).

The mean HALP scores in the frail group were significantly lower than those in the robust and prefrail groups ($p < 0.001$ and $p = 0.001$, respectively). Additionally, the HALP score in the prefrail group was lower than that in the robust group ($p = 0.005$; Table 2).

In logistic regression analysis, after adjusting the HALP score for demographic characteristics, comorbidities, geriatric syndromes, and laboratory findings, a statistically significant difference in the HALP score was observed between frail patients and the robust group ($\beta = -0.040$, OR = 0.96, 95% CI = 0.93–0.95; $p = 0.003$; Model 2). Similarly, after adjusting for the same confounding factors, the prefrail group showed a significant association compared with the robust group ($\beta = -0.018$, OR = 0.98, 95% CI = 0.96–0.99; $p = 0.030$ in Model 2) (Table 3). Decreased HALP scores were associated with prefrail and frail older patients compared with robust patients. No evidence of multicollinearity was observed in the regression models for the frailty scale, with variance inflation factor values ranging from 1.04 to 1.12.

Table 1. Comparisons for demographic features, comorbidities, geriatric syndromes, laboratory findings and comprehensive geriatric assessment parameters in terms of frailty status.

	Robust n = 104	Prefrail n = 177	Frail n = 158	*Pall groups	Probust→frail	Probust→prefrail	Prefrail→frail
Demographic features							
Age (mean ± SD)	73.2 ± 5.2	75.1 ± 6.6	78.4 ± 6.7	**<0.001**	**<0.001**	0.074	**0.001**
Gender (female; %)	64.2	67.2	78.0	**0.031**	**0.028**	0.652	**0.024**
Education year (mean ± SD)	6.80 ± 3.82	5.50 ± 3.90	4.26 ± 3.23	**<0.001**	**<0.001**	0.089	0.208
Comorbities and geriatric syndromes (%)							
Hypertension	79.1	70.6	71.2	0.386	0.212	0.183	0.907
Cardiovascular disease	26.9	19.2	23.2	0.332	0.547	0.192	0.363
Chronic lung disease	12.4	18.6	14.9	0.207	0.416	0.258	0.519
Diabetes mellitus	31.3	44.6	41.2	0.170	0.156	0.060	0.443
Parkinson disease	1.5	2.8	16.4	**<0.001**	**<0.001**	0.549	<0.001
Dementia	9.0	16.9	44.9	**<0.001**	**<0.001**	0.116	<0.001
Recurrent falls (in a year)	28.4	36.2	59.9	**<0.001**	**<0.001**	0.251	<0.001
Essential tremor	14.9	30.5	33.3	**0.012**	**0.004**	**0.014**	0.569
Urinary incontinence	46.3	55.9	62.1	0.148	0.060	0.177	0.275
Geriatric depression	26.9	41.2	67.8	**<0.001**	**<0.001**	**0.038**	**<0.001**
Polypharmacy	58.2	64.4	74.6	**0.024**	**0.013**	0.372	**0.038**
Malnutrition	6.0	23.2	61.0	**<0.001**	**<0.001**	**0.002**	**<0.001**
Probable sarcopenia	3.0	34.5	79.5	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Laboratory findings (mean ± SD)							
Hemoglobin (g/L)	129.1 ± 15.24	126.3 ± 14.92	121.5 ± 18.17	**<0.001**	**0.001**	**0.020**	**0.034**
Lymphocyte count (109/L)	2.06 ± 0.59	1.88 ± 0.69	1.75 ± 0.91	**<0.001**	**<0.001**	**0.032**	**0.009**
Platelet count (109/L)	241.68 ± 63.95	259.84 ± 110.65	260.52 ± 90.01	0.484	0.271	0.572	0.412
Glucose (mg/dL)	111.22 ± 31.28	124.27 ± 52.96	121.54 ± 45.87	0.154	0.132	0.567	0.983
eGFR (mL/min/1.73 m^2)	68.87 ± 14.04	70.92 ± 17.67	63.14 ± 19.48	**<0.001**	**0.047**	0.463	**0.004**
Albumin (g/L)	42.5 ± 2.43	41.4 ± 3.12	40.9 ± 2.45	0.789	**<0.001**	0.225	**<0.001**
TSH (mIU/L)	1.67 ± 1.07	1.71 ± 126	2.36 ± 6.09	0.263	0.895	0.717	0.940
Vitamin B12 (ng/L)	329.91 ± 248.77	354.74 ± 276.50	430.07 ± 352.03	0.119	0.118	0.605	0.084
Folate (mcg/L)	9.50 ± 3.98	8.98 ± 4.55	8.94 ± 4.98	0.722	0.098	0.544	0.852
25-hydroxy vitamin D (mcg/L)	24.28 ± 16.78	21.25 ± 13.09	21.37 ± 14.87	0.308	0.116	0.364	0.888

*Pall groups: comparison for between frail, prefrail and robust group.
eGFR: Estimated glomerular filtration rate, GDS: Geriatric depression scale, MNA-SF: Mini nutritional assessment-short form, POMA: Performance-oriented mobility assessment, SD: Standard deviation, TSH: Thyroid stimulating hormone, TUG: Timed up and go, HALP: Haemoglobin, albumin, lymphocyte and platelet.

Table 2. Comparison for HALP score within robust, prefrail and frail groups.

		p < 0.001		
		p = 0.005	p = 0.001	
		Robust	**Prefrail**	**Frail**
HALP score	Mean	50.79	42.06	35.07
	Standard deviation	21.90	19.17	14.58
	Median	48.30	38.63	34.92
	Interquartile range	27.10	21.50	21.29

HALP: Haemoglobin, albumin, lymphocyte and platelet.

Table 3. Examining the relationship between HALP score in frail and prefrail groups compared to robust group in logistic regression analysis.

		Frail vs. Robust				**Prefrail vs. Robust**			
		β	OR	95 % CI	p	β	OR	95 % CI	p
HALP score	Model 0	-0.031	0.96	0.95–0.98	**<0.001**	-0.020	0.98	0.96–0.99	**0.007**
	Model 1	-0.028	0.97	0.95–0.98	**<0.001**	-0.019	0.98	0.96–0.99	**0.011**
	Model 2	-0.040	0.96	0.93–0.98	**0.003**	-0.018	0.98	0.96–0.99	**0.030**

Model 0- Unadjusted,
Model 1- Adjusted for age and gender,
Model 2- Model 1 plus the presence of Parkinson's disease, dementia, recurrent falls, essential tremor, geriatric depression, polypharmacy, probable sarcopenia.
HALP: Haemoglobin, albumin, lymphocyte and platelet, CI: Confidence interval, OR: Odds ratio.

Discussion

The HALP score was significantly lower in both frail and prefrail patients than in robust older adults in this study. Importantly, this reduction persisted even at the prefrail stage after adjustment for demographic variables, comorbidities, geriatric syndromes, and laboratory findings.

The prevalence of anaemia, defined by reduced red blood cell count or haemoglobin concentration, increases with advancing age (23). Anaemia in older adults can be categorised into the following groups: nutritional anaemia, anaemia due to bleeding, anaemia of chronic disease, anaemia due to haematological malignancy, hereditary anaemia, and unexplained anaemia. Age-related inflammation is associated with anaemia in the elderly; ageing processes such as genomic instability, mitochondrial reactive oxygen species, proinflammatory cytokines, adverse environmental factors, and chronic diseases contribute to this inflammation (24). Additionally, malnutrition, eating disorders, and loss of appetite can lead to anaemia in older adults. Anaemia in this population is associated with increased hospitalisation, falls, dementia, and functional dependence; decreased quality of life; and development of frailty (25). Furthermore, the literature has highlighted a potentially strong association between haemoglobin concentration and frailty (25).

Albumin levels are influenced by patients' nutritional status and metabolic demands (26). Low albumin levels are seen in patients with poor nutritional status and inflammation (27); hence, albumin is considered a negative acute-phase reactant. Increased proinflammatory cytokines, particularly in the context of low albumin levels, are known to significantly contribute to the development of cancer cachexia (26). As a result, it is unsurprising that muscle strength or mass may also be affected in these patients. Inadequate nutritional intake raises the risk of oxidative stress, chronic diseases, impaired immune response, osteoporosis, fracture, peripheral arterial disease, and frailty in older adults (28). Furthermore, malnutrition shares common pathophysiological mechanisms with frailty. The literature also highlights the importance of nutritional support in slowing or preventing frailty (28).

Lymphocytes and platelets are essential mediators of immune function. Decreased lymphocyte levels and increased platelet levels indicate impaired immunity and increased risk of infection (29). Lymphocytes play a key role in the initiation and progression of atherosclerosis (12). For example, lymphopaenia has been associated with inflammation, malnutrition, peripheral congestion, and sympathetic activation in individuals with heart failure (30), while lymphocytes are crucial for immunosurveillance, tumour detection, and destruction in patients with cancer (26). Additionally, a decreased lymphocyte count may be a determinant of unfavourable outcomes in systemic inflammatory diseases (31). The Total lymphocyte count declines with age due to immunosenescence, increasing susceptibility to infections in older adults (32). Thus, changes in lymphocyte counts may be particularly significant in frail individuals. A recent review indicated that low lymphocyte counts may be associated with frailty and its severity (32).

Platelets play an essential role in the progression of acute and chronic diseases, particularly cardiovascular disease, and platelet count generally decreases with age (33). However, the effect of age on platelet function or molecular changes remains unclear (33). A small study examining the relationship between frailty and platelets found greater platelet aggregation and activation in frail individuals (34). Additionally, platelet oxidative stress is thought to increase the risk of cardiovascular disease in frail individuals (35).

The HALP score is a simple, inexpensive, and reliable marker reflecting the combination of inflammation and nutritional status (36). It is a relatively new marker used to assess clinical outcomes and disease progression across a range of conditions. The importance of the HALP score in predicting prognosis was first highlighted in patients with gastric carcinoma (22). Since then, the HALP score has gained attention as a marker of mortality in numerous malignancies and in stroke patients (12). A higher HALP score has been associated with lower mortality in patients with solid tumours or acute ischaemic stroke (30), whereas a low HALP score has been associated with a poorer immunonutritional status (29). In summary, the association of the HALP score with inflammatory conditions is well established. Thus, the lower HALP scores observed among frail individuals in our study suggest that malnutrition and inflammation play a significant role in the aetiopathogenesis of frailty (6,9).

Currently, few studies have evaluated the effectiveness of the HALP score in predicting geriatric syndromes among community-dwelling older adults. In a study of a specific patient population, the HALP score was identified as a risk factor for post-stroke cognitive impairment (31). Another study found that a low HALP score was associated with sarcopenia in patients with intrahepatic cholangiocarcinoma (37). Our findings suggest that the HALP score is associated with prefrailty and frailty according to the Fried criteria, particularly among individuals without malignancy, constituting the first such evidence in the literature.

The pathophysiological mechanisms of frailty remain unclear. However, aging or a low-grade inflammatory status is an important condition in the development of frailty (10). In mouse models, some changes at the genetic, epigenetic, cellular, and systemic levels may play an important role in the development of frailty (38). At the genetic level, deficiencies in the genes Nrf2, which has an important role in the inflammatory pathway, and interleukin (IL)-10, known as an anti-inflammatory cytokine, accelerated frailty in mouse models (38). In addition, chronic inflammation plays a pivotal role in the development of frailty (6). In particular, the production of proinflammatory cytokines, with IL-6 at the forefront, and of chemokines that upregulate IL-6 plays an important role in frailty (38). Oxidative stress, mitochondrial dysfunction, neuroendocrine dysregulation, and inflammation also contribute to the anorexia of aging, indicating the relationship between frailty and malnutrition (38,39). Therefore, the early predictive power of the HALP score may be important because of these mechanisms. An important finding of this study is that the HALP score was already significantly lower in the prefrail group than in robust older adults, even after adjustment for confounding factors. This suggests that deterioration in immunonutritional status may begin at the prefrailty stage, before overt frailty becomes clinically apparent. Given that prefrailty represents a potentially reversible state, the observed early decline in HALP may reflect subclinical inflammation, early malnutrition, or immune dysregulation, all of which may precede functional decline. Therefore, HALP may capture biological vulnerability at a stage when preventive interventions could still be effective.

Inflammaging, defined as chronic, low-grade inflammation associated with aging, increases the risk of mortality and morbidity (40). C-reactive protein and IL-6 are at the forefront of inflammation in the elderly (40). It is known that inflammation is also associated with malnutrition in older adults (41). Nutritional assessment can predict frailty (42). As a result, frailty and malnutrition share common pathophysiological mechanisms and are closely related. Because the HALP score provides information relevant to nutritional assessment, low HALP scores in frail older individuals support an association with both malnutrition and inflammation.

Study Limitations

This study has several important methodological limitations that should be acknowledged when interpreting the findings. First, its retrospective, cross-sectional design precludes causal inference regarding the association between the HALP score and frailty status. Second, although we adjusted for multiple demographic, clinical, and geriatric confounders in multivariable models, residual confounding cannot be excluded. In particular, factors such as hydration status, the acute-phase response, medication use, and subclinical inflammation may influence hemoglobin and albumin levels, and thereby affect the HALP score independently of frailty. Third, our strict exclusion criteria, including patients with advanced chronic kidney disease, malignancy, severe anemia, acute infection, and major cardiovascular or neurological conditions, may have resulted in selection bias and may have limited the generalizability of our findings to the broader older adult population. Consequently, the observed associations may not fully represent medically complex or hospitalized older adults. Fourth, although frailty was assessed using the Fried phenotype and a CGA was performed, formal neurocognitive testing, such as the Mini-Mental State Examination was not available, which limits the interactions among cognitive impairment, HALP score, and frailty. Finally, as laboratory measurements were obtained at a single time point, intra-individual biological variability and transient changes in

hematologic or nutritional parameters could not be accounted for. Therefore, HALP should be interpreted as a risk stratification marker rather than a definitive diagnostic or causal biomarker of frailty.

Conclusion

The HALP score appears to be a simple and inexpensive biomarker associated with frailty and may be useful for risk stratification in clinical settings; however, its predictive value should be confirmed in prospective longitudinal studies.

References

1. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381:752-762.
2. Doody P, Lord JM, Greig CA, Whittaker AC. Frailty: Pathophysiology, theoretical and operational definition(s), impact, prevalence, management and prevention, in an increasingly economically developed and ageing world. Gerontology. 2023;69:927-945.
3. Aznar-Tortonda V, Palazón-Bru A, Gil-Guillén VF. Using the frail scale to compare pre-existing demographic lifestyle and medical risk factors between non-frail, pre-frail and frail older adults accessing primary health care: a cross-sectional study. PeerJ. 2020;8:e10380.
4. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56:M146-M156.
5. Aznar-Tortonda V, Palazón-Bru A, la Rosa DMF, Espínola-Morel V, Pérez-Pérez BF, León-Ruiz AB, Gil-Guillén VF. Detection of frailty in older patients using a mobile app: cross-sectional observational study in primary care. Br J Gen Pract. 2019;70:e29-e35.
6. Kim DH, Rockwood K. Frailty in older adults. N Engl J Med. 2024;391:538-548.
7. Kocyigit SE, Ates Bulut E, Aydin AE, Dost FS, Kaya D, Isik AT. The relationship between cognitive frailty, physical frailty and malnutrition in Turkish older adults. Nutrition. 2024;126:112504.
8. Palmer K, Vetrano DL, Marengoni A, Tummolo AM, Villani ER, Acampora N, Bernabei R, Onder G. The relationship between anaemia and frailty: a systematic review and meta-analysis of observational studies. J Nutr Health Aging. 2018;22:965-974.
9. Ni Lochlainn M, Cox NJ, Wilson T, Hayhoe RPG, Ramsay SE, Granic A, Isanejad M, Roberts HC, Wilson D, Welch C, Hurst C, Atkins JL, Mendonça N, Horner K, Tuttiett ER, Morgan Y, Heslop P, Williams EA, Steves CJ, Greig C, Draper J, Corish CA, Welch A, Witham MD, Sayer AA, Robinson S. Nutrition and frailty: opportunities for prevention and treatment. Nutrients. 2021;13:2349.
10. Bleve A, Motta F, Durante B, Pandolfo C, Selmi C, Sica A. Immunosenescence, inflammaging, and frailty: role of myeloid cells in age-related diseases. Clin Rev Allergy Immunol. 2023;64:123-144.
11. Arauna D, Navarrete S, Albala C, Wehinger S, Pizarro-Mena R, Palomo I, Fuentes E. Understanding the role of oxidative stress in platelet alterations and thrombosis risk among frail older adults. Biomedicines. 2024;12:2004.
12. Pan H, Lin S. Association of hemoglobin, albumin, lymphocyte, and platelet score with risk of cerebrovascular, cardiovascular, and all-cause mortality in the general population: results from the NHANES 1999-2018. Front Endocrinol (Lausanne). 2023;14:1173399.
13. Zeng M, Li Y, Zhu Y, Sun Y. Inflammatory markers and clinical factors as key independent risk factors for frailty: a retrospective study. BMC Geriatr. 2025;25:404.
14. Sachdev PS, Blacker D, Blazer DG, Ganguli M, Jeste DV, Paulsen JS, Petersen RC. Classifying neurocognitive disorders: the DSM-5 approach. Nat Rev Neurol. 2014;10:634-642.
15. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48:16-31.
16. Guigoz Y. The Mini Nutritional Assessment (MNA) review of the literature--What does it tell us? J Nutr Health Aging. 2006;10:466-485; discussion 485-487.
17. Durmaz B, Soysal P, Ellidokuz H, Isik AT. Validity and reliability of geriatric depression scale-15 (short form) in Turkish older adults. North Clin Istanb. 2018;5:216-220.
18. Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. J Am Geriatr Soc. 1986;34:119-126.
19. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39:142-148.
20. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL index: a reliability study. Int Disabil Stud. 1988;10:61-63.
21. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969;9:179-186.
22. Chen XL, Xue L, Wang W, Chen HN, Zhang WH, Liu K, Chen XZ, Yang K, Zhang B, Chen ZX, Chen JP, Zhou ZG, Hu JK. Prognostic significance of the combination of preoperative hemoglobin, albumin, lymphocyte and platelet in patients with gastric carcinoma: a retrospective cohort study. Oncotarget. 2015;6:41370-41382.
23. Stauder R, Valent P, Theurl I. Anemia at older age: etiologies, clinical implications, and management. Blood. 2018;131:505-514.
24. Wacka E, Nicikowski J, Jarmuzek P, Zembron-Lacny A. Anemia and its connections to inflammation in older adults: a review. J Clin Med. 2024;13:2049.
25. Steinmeyer Z, Delpierre C, Soriano G, Steinmeyer A, Ysebaert L, Balardy L, Sourdet S. Hemoglobin concentration; a pathway to frailty. BMC Geriatr. 2020;20:202.
26. Farag CM, Antar R, Akosman S, Ng M, Whalen MJ. What is hemoglobin, albumin, lymphocyte, platelet (HALP) score? A comprehensive literature review of HALP's prognostic ability in different cancer types. Oncotarget. 2023;14:153-172.
27. Eckart A, Struja T, Kutz A, Baumgartner A, Baumgartner T, Zurfluh S, Neeser O, Huber A, Stanga Z, Mueller B, Schuetz P. Relationship of Nutritional Status, Inflammation, and serum albumin levels during acute illness: a prospective study. Am J Med. 2020;133:713-722.e7.
28. Lorenzo-López L, Maseda A, de Labra C, Regueiro-Folgueira L, Rodríguez-Villamil JL, Millán-Calenti JC. Nutritional determinants of frailty in older adults: A systematic review. BMC Geriatr. 2017;17:108.
29. Antar R, Farag C, Xu V, Drouaud A, Gordon O, Whalen MJ. Evaluating the baseline hemoglobin, albumin, lymphocyte, and platelet (HALP) score in the United States adult population and comorbidities: an analysis of the NHANES. Front Nutr. 2023;10:1206958.
30. Liu L, Gong B, Wang W, Xu K, Wang K, Song G. Association between haemoglobin, albumin, lymphocytes, and platelets and mortality in patients with heart failure. ESC Heart Fail. 2024;11:1051-1060.
31. Zuo L, Dong Y, Liao X, Hu Y, Pan Y, Yan H, Wang X, Zhao X, Wang Y, Seet RCS, Wang Y, Li Z. Low HALP (hemoglobin, albumin, lymphocyte, and platelet) score increases the risk of post-stroke cognitive impairment: a multicenter cohort study. Clin Interv Aging. 2024;19:81-92.

32. Navarro-Martínez R, Cauli O. Lymphocytes as a biomarker of frailty syndrome: a scoping review. Diseases. 2021;9:53.

33. Jones CI. Platelet function and ageing. Mamm Genome. 2016;27:358-366.

34. Hernández B, Fuentes E, Palomo I, Alarcón M. Increased platelet function during frailty. Exp Hematol. 2019;77:12-25.e2.

35. Fuentes F, Palomo I, Fuentes E. Platelet oxidative stress as a novel target of cardiovascular risk in frail older people. Vascul Pharmacol. 2017;93–95:14–19.

36. Yuan Y, Liang X, He M, Wu Y, Jiang X. Haemoglobin, albumin, lymphocyte, and platelet score as an independent predictor for renal prognosis in IgA nephropathy. Front Endocrinol (Lausanne). 2024;15:1339921.

37. Toshida K, Itoh S, Nakayama Y, Tsutsui Y, Kosai-Fujimoto Y, Tomino T, Yoshiya S, Nagao Y, Harada N, Kohashi K, Oda Y, Yoshizumi T. Preoperative HALP score is a prognostic factor for intrahepatic cholangiocarcinoma patients undergoing curative hepatic resection: association with sarcopenia and immune microenvironment. Int J Clin Oncol. 2023;28:1082-1091.

38. Liu P, Li Y, Ma L. Frailty in rodents: Models, underlying mechanisms, and management. Ageing Res Rev. 2022;79:101659.

39. Park C, Ko FC. The science of frailty: sex difference. Clin Geriatr Med. 2021;37:625-638.

40. Franceschi C, Campisi J. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. J Gerontol A Biol Sci Med Sci. 2014;69 Suppl 1:S4-S9.

41. Stumpf F, Keller B, Gressies C, Schuetz P. Inflammation and nutrition: friend or foe? Nutrients. 2023;15:1159.

42. Soysal P, Isik AT, Arik F, Kalan U, Eyvaz A, Veronese N. Validity of the mini-nutritional assessment scale for evaluating frailty status in older adults. J Am Med Dir Assoc. 2019;20:183-187.