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RESEARCH ARTICLE

From Inflammation to Frailty: Investigating the Systemic Immunity-Inflammation Index in Older Patient

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Abstract

Introductıon: Chronic inflammation is increasingly recognized as a crucial contributor to frailty pathogenesis, but accurate diagnosis remains a challenge. Aim Our study aims to investigate the relationship between frailty and the Systemic Immunity-Inflammation Index (SII, SIRI), a comprehensive indicator of inflammation.

Methods: This cross-sectional study enrolled 200 patients. All participants underwent a comprehensive geriatric assessment. Frailty was assessed using the clinical frailty scale, (≥ 4; frail, <4 robust). 99 patients were included in the study as frail (Group 1) and 101 patients as robust (Group 2). To determine the SII, we used the formula: Platelet count×Neutrophil / Lymphocyte count. The calculation formula for SIRI is neutrophil count × monocyte count/Lymphocyte count.

Results: The average age of the participants was 75.15 ± 8,8, and 55% (n=110) were female. Patients were grouped frail and robust. The frail group had 99 patients, while the robust group comprised 101 patients. Frail patients showed higher median SII and SIRI scores than the robust group($p < 0.001$). Bınary logistic regression analysis revealed that the SII and SIRI scores were significantly and independently associated with frailty even after adjusting for potential confounding factors respectively (r =1.52, 95% CI= 1.189–1.964, $p < 0.001$, r=1.004, 95% CI=0.585-1.724, p=0.987). The ROC analysis identified the optimal cut-off for SII in predicting sarcopenia as > 596. At this threshold, the negative predictive values were determined to be 83.8%, with a specificity of 86%, cut-off for SIRI in predicting sarcopenia as > 1.1 .

Conclusion: The results of this cross-sectional study indicate a positive correlation between systemic inflammatory biomarkers (SII, SIRI) and frailty.

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Introduction

Frailty is a complex condition that can significantly reduce survival rates at any age and is associated with progressive impairments across multiple physiological systems due to aging.[1]

Blood inflammatory markers are readily available and reasonably priced biomarkers. Systemic Immunity-Inflammation Index(SII) is a reliable and consistent measure that integrates three different types of inflammatory cells (lymphocytes, neutrophils, and platelets) and can be used as indications of both systemic inflammation and local immune response.[2,3] The SII can predict the prognosis of patients with a variety of malignancies, acute ischemic stroke, coronary artery disease, and acute renal injury, according to multiple research studies.[4] Systemic ınflammatory Response Index(SIRI) is a more complete measure of chronic inflammation since it comprises neutrophils, monocytes, and lymphocytes.[5] Furthermore, prior studies have discovered a link between frailty and interleukin-6 and C-reactive protein.[6] Several studies have linked systemic inflammatory biomarkers to the likelihood of frailty.[7] Pathophysiological changes occurring in several systems, including the cardiovascular, endocrine, immunological, and musculoskeletal systems, contribute to the development of frailty syndrome.[8]

This study specifically focused on geriatric assessment and aims to evaluate the relationship between frailty in older adults and the SII and the SIRI

Material and Methods

Study design

Features of the population, BMI, multimorbidities(≥1 medical condition), smoking status, and biochemical results were recorded. Patients under 65, current smokers, and those with alcohol or drug addiction were excluded. Between January 2025 and February 2025, 200 patients aged 65 and over were retrospectively scanned and geriatric evaluations and CBC scans were performed. Education level was categorized as 0 = 0–5 years, 1 = 6–12 years, and 2 = >12 years.

Comprehensive geriatric evaluation

The Lawton-Brody Instrumental Activities of Daily Living (IADL) and Katz Activities of Daily Living (ADL) were used to assess the functional condition of the subjects. Katz's ADL assessment consisted of six questions on how independently the patient performed basic care and everyday duties. The score dropped as independence increased.[9] The IADL evaluates individuals' capacity to do complicated everyday tasks, and the rating is determined by adding up to eight points.[10] The Mini-Nutritional Assessment Short Form (MNA-SF) was used to assess the individual's nutritional status and malnutrition was indicated by ≤7 points.[11] Additionally, the number of drugs was noted, and using more than five was deemed to be polypharmacy.[12]

Frailty assessment

The same experienced doctor evaluated patients' frailty state using the Clinical Frailty Scale (CFS). Clinical frailty is defined by CFS using a scoring system that ranges from 1 (extremely fit) to 9 (terminally ill), live with frailty (CFS ≥4), and being non-frail/robust (CFS < 4).[13,14]

Systemic inflammatory biomarkers

All participants underwent a comprehensive blood analysis after an overnight fast on the same day as theirs. This analysis included a complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) measurement. CBC was performed with a Beckman Coulter automated analyzer. SII was assessed according to the formula: Platelet count(109/mm3)×Neutrophil count (109/mm3) / Lymphocyte count (109/mm3).[15] The calculation formula for SIRI is Neutrophil count × Monocyte count/Lymphocyte count.[16]

Statistical analyses

Version 23 of the SPSS software was used to perform the statistical analysis. The variables were examined visually and analytically to see if they were regularly distributed. Descriptive analyses were presented as percentages for categorical variables, mean ± SD for normally distributed variables, and median [interquartile range (IQR)] for non-normally distributed variables. The Chi-square test was employed to compare the category variables. The continuous variables were compared using the Mann-Whitney U test. Using two-sided tests, all reported p-values were computed and compared to a 5% significance level. ROC analysis was performed to determine the cut-offs of the available indices and analyzed by logistic binary regression to exclude confounding factors.

Results

A total of 200 individuals aged 65 years and older were included in this cross-sectional study. The mean age of the participants was 75.15 ± 8.8 years, and 55% were female.The cohort was separated into

two groups according to frailty state, with 99 patients (45%) defined as frail (Group-1) and 101 patients (50.5%) as robust (Group-2). Table 1 shows that patients living with frailty have a considerably higher mean age (79.75 ± 3.43 years) than the robust group (72.71 ± 5.8 years, p < 0.001).

Table 1. The baseline characteristics of the patients are frail and robust.

	Frail (n=99)	Robust (n=101)	p
Age, years	79.75±3.43	72.71.±5.8	<0.001
Marital status, Married	81(63.8)	30(53.6)	0.170
Sex, Female	46(46)	61 (61)	0.037
Education level			0.585
0	55(55)	49 (50)	
1	33 (33)	28 (29)	
2	18(18)	19 (20)	
Height, cm	165 [14]	159 [9.5]	0.129
Polypharmacy, n (%)	80(80)	53(53)	0.001
Weight, kg	65[15]	74 [15.4]	0.50
BMI, kg/m2	24.5±5.2	28.9±5.9	0.443
Katz Activities of Daily Living	4(0-6)	6(0-6)	0.001
Lawton Instrumental Activities of Daily Living	5(0-8)	7(0-8)	0.001
SII	942 (137-9710)	250 (190-440)	<0.001
SIRI	1.5(0.11-14)	0.99(0.6-1.5)	<0.001

*Variables are presented as n (%), mean±SD or median [IQR]
BMI, Body mass index; cm, centimeter; kg, Kilogram; kg/m2., Kilogram/square meters; SII, Systemic Immunity-Inflammation Index; SIRI, Systemic Inflammation Response Index

Frail individuals had a higher prevalence of polypharmacy (80% vs. 53% in robust patients, p < 0.001) and scored significantly lower on both Katz Activities of Daily Living (ADL) and Lawton Instrumental Activities of Daily Living (IADL) assessments (p < 0.001). The frail group had significantly higher Systemic Immunity-Inflammation Index (SII) and Systemic Inflammatory Response Index (SIRI) scores than the robust group (SII: p < 0.001; SIRI: p < 0.001).

After correcting for relevant confounders, binary logistic regression analysis showed that SII and SIRI were independently linked with frailty (OR=1.52; 95% CI, 1.189-1.964; p < 0.001; OR=1.004; 95% CI, 0.585-1.724; p=0.987) (Table 3). ROC analysis revealed the appropriate cut-off values for predicting frailty; The SII demonstrated excellent discriminatory ability, with an AUC of 0.895 (95% CI: 0.851–0.940, p < 0.001), suggesting a high level of accuracy in distinguishing between affected and non-affected individuals. The optimal cut-off value for SII was 596, yielding a sensitivity of 83.8% and a specificity of 86.1%, indicating robust diagnostic performance.

Table 3. Association of SII and SIRI with Frailty: Binary Logistic Regression Results

	Odds Ratio	95 % CI	p
Unadjusted Model			
SII	1.005	1.003-1.006	<0.001
Model 1			
SII	1.52	1.189-1.964	<0.001
SIRI	1.004	0.585-1.724	0.987
Age, years	1.111	1.075-1.273	<0.001
BMI (kg/m2)	0.826	0.721-0.945	0.006

BMI, Body mass index; SII, Systemic Immunity-Inflammation Index; SIRI, Systemic Inflammation Response Index; CI: Confidence Interval; kg/m2., Kilogram/square meters

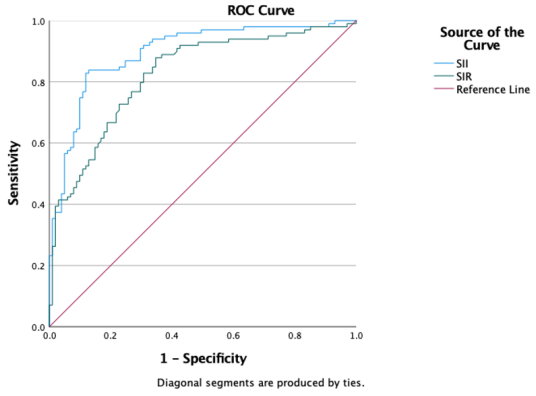
Similarly, the SIRI exhibited strong predictive power, with an AUC of 0.823 (95% CI: 0.765–0.881, p < 0.001). The best cut-off value for SIRI was 1.1, with a sensitivity of 84.7% and specificity of 85.3% (Table 2, Figure-1).

Table 2. Diagnostic Performance of SII and SIRI in Predicting Frailty: ROC Curve Analysis

	Cut-off	AUC	Sensitivity	Specificity	95% CI	p
SII	596	0.895	83.8%	86.1%	0.851-0.940	<0.001
SIRI	1.1	0.823	84.7%	85.3%	0.765-0.881	<0.001

ROC, Receiver Operating Characteristic Curve; AUC, Area Under the Curve; CI, Confidence Interval; SII, Systemic Immunity-Inflammation Index; SIRI, Systemic Inflammation Response Index

Figure-1 The ROC Curve of the Systemic Immunity -Inflammation IndexS



SII, Systemic Immunity-Inflammation Index; SIRI, Systemic Inflammation Response Index; ROC, Receiver Operating Characteristic Curve

Discussion

This study provides strong evidence linking systemic inflammatory biomarkers, particularly the SII and the SIRI, to frailty in older adults. Our findings reinforce the expanding literature suggesting that chronic low-grade inflammation plays a central role in the development of frailty. Notably, frail individuals exhibited significantly higher levels of SII and SIRI compared to their robust counterparts, highlighting the potential of these markers as objective indicators of frailty risk. These results align with previous research indicating that systemic inflammatory markers, such as IL-6 and CRP, are associated with frailty and negative health outcomes in aging populations. The inflammatory load in frail individuals appears to be a key determinant of increased vulnerability, reinforcing the need for targeted therapeutic approaches.[17]

Frailty is a complex geriatric syndrome characterized by increased vulnerability to external stressors due to physiological dysregulation.[18]

Our results indicate that heightened systemic inflammation may contribute to functional decline, as reflected in lower ADL and IADL scores among frail participants. This aligns with prior findings that inflammation-driven muscle catabolism, immune senescence, and metabolic alterations lead to declines in physical and cognitive function, further exacerbating frailty. A recent systematic review confirmed that inflammatory cytokines such as IL-6 and tumor necrosis factor-alpha negatively impact muscle strength and mobility, directly influencing frailty progression.[19] Additionally, the higher prevalence of polypharmacy among frail individuals in our study corresponds with evidence suggesting that polypharmacy is both a consequence and a risk factor for frailty.

Given that polypharmacy may induce adverse drug reactions and exacerbate inflammatory responses, future research should explore interventions aimed at optimizing medication use in frail populations.[20]

One of the key contributions of our study is the identification of clinically meaningful cut-off values for SII and SIRI. These findings are in agreement with prior research that has established SII and SIRI as predictive markers of inflammation-driven diseases, including cardiovascular disease, cancer, and metabolic disorders.[21]

The ability of these indices to predict frailty further supports their clinical utility as cost-effective, widely available biomarkers that could enhance risk assessment in geriatric practice.[22] In line with our findings, a recent study by Alhalwani found that elevated SII levels correlated with disease severity in type 2 diabetes mellitus, another condition associated with frailty.[23] These findings highlight the potential of systemic inflammation indices in risk stratification and disease monitoring across different aging-related conditions.

Interestingly, while both SII and SIRI were initially associated with frailty in unadjusted analyses, binary logistic regression revealed that only SII maintained statistical significance after controlling for confounding variables. This suggests that SII may be a more robust predictor of frailty than SIRI, warranting further investigation. Prior studies have highlighted the role of platelets in aging and frailty, suggesting that platelet-mediated inflammation may play a more significant role in frailty pathogenesis than monocyte-driven responses, which could explain our findings Moreover, a study) demonstrated that SII is linked to increased urinary albumin excretion, reinforcing the systemic impact of chronic inflammation in aging individuals.[24,25]

Future longitudinal studies should investigate whether reductions in inflammatory markers over time correspond with decreased frailty risk, offering further insights into causality.

These findings have important clinical implications. Given the modifiable nature of inflammation, future research should explore targeted interventions aimed at mitigating inflammatory burden in older adults. Studies have shown that lifestyle modifications, including regular physical activity, anti-inflammatory dietary patterns, and pharmacological interventions (e.g., statins and metformin), may help reduce systemic inflammation and delay frailty onset.[26,27]

Additionally, incorporating SII and SIRI into routine geriatric assessments could provide valuable prognostic information, enabling early identification of high-risk individuals and facilitating timely interventions. The integration of systemic inflammatory indices in clinical practice may allow for the implementation of personalized medicine approaches, optimizing patient care and outcomes in aging populations.

Conclusion

Our study highlights the pivotal role of systemic inflammation in frailty pathophysiology and positions SII and SIRI as valuable biomarkers in geriatric assessments. These findings add to the growing evidence supporting the use of inflammatory indices in predicting frailty and suggest that inflammation-targeted strategies may help improve health outcomes in aging populations. Future research should focus on validating these findings in larger, diverse cohorts and exploring novel therapeutic approaches aimed at modulating systemic inflammation to promote healthy aging. Given the increasing global burden of frailty, the identification of reliable, cost-effective biomarkers such as SII and SIRI represents a crucial step forward in geriatric medicine, offering potential avenues for early intervention and improved patient outcomes.

Conflict of Interest: The authors declare no conflict of interest.

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Ethics Statement: The study protocol, ID: TABED-2-25-1072, was approved by XXX Hospital's Ethics Committee. Since this was a retrospective cross-sectional study, written informed consent was waived. The study adhered to the principles of the Declaration of Helsinki.

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