FRAIL Scale: an independent predictor of in-hospital mortality among older adults

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Abstract. – OBJECTIVE: To screen for geriatric syndromes in older in-hospital patients and investigate their relationship with mortality.

PATIENTS AND METHODS: Demographic data, comorbidities, and medical history of the patients were recorded. Anthropometric measurements were obtained at 72 hours after hospital admission. The Mini Nutritional Assessment-Short Form, strength, assistance with walking, rising from a chair, climbing stairs, and falls (SARC-F) sarcopenia screening questionnaire, Katz Activities of Daily Living scale, Lawton-Brody instrumental activities of daily living scale, the fatigue, resistance, ambulation, illness, and loss of weight (FRAIL) scale and the Eating Assessment Test-10 (EAT-10) screening test were used to assess geriatric syndromes. All patients were evaluated for delirium, pain, falls, polypharmacy, sleep disorders, incontinence, and pressure injury by the same researcher.

RESULTS: A total of 85 patients were included in the study. The mean age was 75±7 years (range: 66-97). During hospital follow-up, 15.3% (n=13) of the patients died and 84.7% (n=72) were discharged. The median length of stay was 19 days (range: 3-126 days). In the multivariate analysis, frailty (hazard ratio: 2.67, 95% CI: 1.41-5.06, *p*=0.003) was found to be associated with in-hospital mortality.

CONCLUSIONS: Frailty is an independent risk factor for in-hospital mortality in older adults.

Key Words:
Frailty, Geriatric syndromes, In-hospital mortality.

Introduction

The age structure of the population is changing worldwide, with the older population growing every year. Geriatric assessment requires an intensive, multidisciplinary approach because of the complex and interrelated problems older people face. Therefore, the evaluation of older patients is referred to as "multidimensional geriatric assessment" and includes functional, physical, social, environmental, and psychological evaluations.

The presence of geriatric syndromes accompanying chronic diseases leads to higher mortality and morbidity[1,2]. This increases the importance of identifying risk factors for the development of geriatric syndromes, taking preventive measures, and developing effective treatment strategies[3]. Common geriatric syndromes include pain[4], falls and fear of falling, pressure injury, incontinence, delirium, depression[5], dementia, sleep disorders, polypharmacy, malnutrition, sarcopenia[2], functional impairment, frailty, and dysphagia[6].

Infection, stroke, myocardial infarction, diabetes, and cancer have been identified as the most important factors contributing to in-hospital mortality in older patients. However, more comprehensive studies[7,8] have shown that many other factors, such as poor functional capacity and cognitive status, delirium, malnutrition, frailty, pressure injury, depression, and dementia, also have a significant effect on mortality.

The aim of this study was to investigate the effect of geriatric syndromes on mortality in patients over 65 years of age who were hospitalized.

Patients and Methods

Patients aged 65 years and older who were hospitalized between September 2021 and January 2022 were included in this cross-sectional study. In accordance with the ethical principles of the Declaration of Helsinki, the study included volunteers who agreed to participate in the study and provided informed consent (for patients with dementia and delirium, informed consent was ob-

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tained from their relatives). Individuals who did not give informed consent and were hospitalized for less than 72 hours were not included. The study was approved by the University Clinical Research Ethics Committee (protocol code: 09.2021.934).

As the in-hospital mortality rate in the geriatric population was reported to be 12-35% in the literature, to make a prediction for these patients with a 7% error (to find a mortality rate of 23-37%), the minimum sample size for type 1 error of 0.05, type 2 error of 0.20, and power of 0.80 was calculated as 68 patients. Based on this calculation, we included 85 inpatients (42 women, 43 men) in the study.

Within the scope of the comprehensive geriatric assessment, the patients' demographic information, comorbidities, and medical history were questioned, and their anthropometric measurements were obtained 72 hours after hospital admission. All patients were evaluated for delirium, pain, falls, polypharmacy, sleep disorders, incontinence, and pressure injury by the same researcher. Laboratory blood values after admission were included in the study.

Body mass index (BMI) was calculated using height and weight data as body weight (kg)/height^2 (m^2). Calf circumference and mid-upper arm circumference measurements were performed using a tape measure. A calf circumference threshold of 33 cm was used to define low muscle mass in the Turkish population as per the definition of the European Working Group on Sarcopenia in Older People[9].

The Mini Nutritional Assessment-Short Form (MNA-SF) is a screening test with a maximum score of 14 points. MNA-SF scores of 0-7 are interpreted as malnutrition, 8-11 as malnutrition risk, and scores above 11 as normal nutritional status[10]. During the study, additional nutritional support was provided, and dietary recommendations were made to patients with malnutrition or risk of malnutrition, according to the MNA-SF.

The strength, assistance with walking, rising from a chair, climbing stairs, and falls (SARC-F) questionnaire is a sarcopenia screening test consisting of 5 questions scored from 0 to 2 points. Scores of 4 and higher are considered significant in terms of sarcopenia[11]. During the study, sarcopenic patients were given in-bed or out-of-bed exercises and nutritional support.

The Katz activity of daily living (ADL) scale consists of 6 questions including basic ADL such as bathing, dressing, toileting, transferring from bed, continence, and eating. Patients with scores in the range of 0-6 points are considered dependent, those in the range of 7-12 points are considered semi-independent, and those at 13 points and above are considered completely independent. The Lawton-Brody instrumental ADL scale consists of 8 questions scored from 1 to 3. Scores of 0-8 indicate dependence, 9-16 as semi-independence, and 17 and higher as independent[12,13].

The fatigue, resistance, ambulation, illness, and loss of weight (FRAIL) scale is used as a frailty assessment test in the geriatric population. The 5 questions in the scale are answered as yes (1 point) or no (0 points). A total score of 0 is interpreted as normal, 1-2 as pre-frail, and 3-5 as frail[14].

The Eating Assessment Test-10 (EAT-10) is a simple screening test that reveals the presence and severity of patients' dysphagia complaints and is easily administered in the clinical setting. The maximum score is 40, and scores of 3 and higher are considered pathological[15]. Polypharmacy was defined as the use of 5 or more drugs[16].

Glomerular filtration rate (GFR) was calculated with the Cockroft-Gault formula. Rates lower than 60 mL/min/1.73 m^2 were interpreted as impaired kidney function, and values at or above this threshold were interpreted as normal kidney function[17].

The patients were categorized into two groups based on whether hospital follow-up ended in discharge or death. Mortality status was ascertained from the hospital information management system.

Statistical Analysis

The study data were analyzed for statistical significance using SPSS Statistics 21.0 (IBM Corp., Armonk, NY, USA) software. Continuous data and descriptive variables were assessed for normal distribution using Kolmogorov-Smirnov/Shapiro-Wilk tests. Mean and standard deviation (SD) values were given for normally distributed variables, and median and range (minimum-maximum) values were given for non-normally distributed variables. Independent-sample *t*-test was used to compare numerical data with normal distribution, and the Mann-Whitney U test was used for numerical data that did not show normal distribution. The Chi-square test was used to compare the effect of categorical variables on in-hospital mortality. Multivariate independent variables were evaluated using Cox regression analysis. All statistical tests were two-tailed and *p*-values lower than or equal to 0.05 were considered statistically significant.

Results

A total of 85 patients were included in the study. Of the patients, 49.4% (n=42) were women. The mean age of the patients was 75.9±7.6 years (66-97). The mean length of hospital stay was 19 days (3-126 days). The most common reason for hospitalization was infectious disease (n=28, 32.9%) and the most common geriatric syndrome was polypharmacy (>5 drugs), at 97.6% (n=83) (Table I). The mean number of drugs used during hospitalization was 11 (4-20).

The patients' mean BMI and mean calf circumference were 24.7±5.7 (13.3-45.8) and 32.5±6.6 cm (15-58), respectively.

Factors Associated with In-Hospital Mortality

The rate of in-hospital mortality was 15.3% (n=13). Those who died were significantly younger than those who survived (72.8±4.5 *vs.* 76.6±7.9, *p*=0.008) (Table II).

A diagnosis of malignancy was significantly associated with mortality during in-hospital follow-up (69.2% *vs.* 38.9%, *p*=0.042). Dementia was not detected in any of the non-survivors (18.1% *vs.* 0%, *p*=0.030). Other chronic diseases had no significant effect on mortality.

All of the non-surviving patients were evaluated as frail, and the prevalence of frailty was significantly associated with mortality (100% *vs.* 78%, *p*=0.015) (Table II).

Table I. Demographic characteristics of internal medicine inpatients over 65 years of age (n=85).

	Participants (n=85), n (%)
Age (years)*	75.9±7.6 (66-97)
Age group	
65-74	43 (50.6)
75-84	28 (32.9)
≥85	14 (16.5)
Gender	
Female	42 (49.4)
Male	43 (50.6)
Number of Chronic Diseases*	5 (1-11)
Diagnosis on Admission	
Infection	28 (32.9)
Malignancy	25 (29.4)
CKD/AKI/Electrolyte Imbalance	9 (10.6)
Pulmonary Embolism	5 (5.9)
Diabetes Mellitus	4 (4.7)
Others	14 (16.5)
Frailty According to FRAIL	
Frail	69 (81.2)
Non-frail	16 (18.8)

*Values were expressed as mean±standard deviation or median (minimum-maximum). AKI: Acute kidney injury, CKD: Chronic kidney disease, FRAIL: Fatigue, Resistance, Ambulation, Illnesses, and loss of Weight.

Independent Risk Factors Associated with In-Hospital Mortality

To determine mortality risk factors, Cox regression analysis was performed with age, sex, frailty, cancer, and calf circumference, which were variables statistically significant in univariate analyses ($p<0.05$). The model revealed that frailty (HR: 2.86, 95% confidence interval: 1.53-5.36, *p*=0.001) was a significant independent variable associated with in-hospital mortality among geriatric inpatients (Table III).

Discussion

This study evaluated the association between geriatric syndromes and in-hospital mortality in older adults. In-hospital mortality rates reported in the literature for geriatric patients range between 12% and 35%[18], and this rate was 15% in our study.

In our study, we observed a higher mortality rate among young-old patients compared to the oldest-old. The burden of disease (especially malignancy, which is associated with a high mortality rate) was greater in the young-old, and this inverse relationship between age and mortality may be explained by the disease burden in non-surviving patients.

In this study, the prevalence of frailty was 81%, consistent with the findings of another study[19] of older internal medicine inpatients that showed this rate could increase up to 87%. Our hospital is also a tertiary health center, and inpatients' higher rates of inadequate ambulation, malnutrition, and dependence may explain the high rates of frailty. Studies[19,20] have shown that the FRAIL scale is more effective in predicting in-hospital mortality. Similarly, multivariate analyses in our study showed that frailty was an independent risk factor for mortality. Mitochondrial dysfunction and chronic inflammation play a role in the frailty-mortality relationship. Age-related decreases in growth hormone, insulin-like growth factor-1, and sex steroids and an increase in cortisol level are involved in the pathogenesis of frailty[21,22].

Table II. Factors Associated with in-hospital mortality and geriatric syndromes.

	Survivors (n=72), n (%)	Non-survivors (n=13), n (%)	*p*-value
Age (years)*	**76.6±7.9**	**72.8±4.5**	**0.008**
Gender			
Female	36 (50.0)	6 (46.2)	0.799
Male	36 (50.0)	7 (53.8)	
Dementia	**13 (18.1)**	**0 (0.0)**	**0.030**
Malignancy	**28 (38.9)**	**9 (69.2)**	**0.042**
Calf Circumference (cm)*	**33.1±6.6**	**28.8±5.4**	**0.030**
Number of Drugs used*	11 (4-20)	11 (6-20)	0.412
Length of hospital stay (days)*	19 (3-126)	25 (7-57)	0.195
Polypharmacy (>5 Drugs)	70 (97.2)	13 (100.0)	0.412
Functionality – ADL			
Dependent	10 (13.9)	3 (23.1)	0.635
Semi-independent	17 (23.6)	2 (15.4)	
Independent	45 (62.5)	8 (61.5)	
Functionality – IADL			
Dependent	10 (13.9)	3 (23.1)	0.406
Semi-independent	20 (27.8)	5 (38.5)	
Independent	42 (58.3)	5 (38.5)	
Malnutrition Status According to MNA-SF			
Malnutrition	37 (51.4)	7 (53.8)	0.369
Malnutrition risk	19 (26.4)	5 (38.5)	
Normal	16 (22.2)	1 (7.7)	
Frailty According to FRAIL			
Frail	**56 (77.8)**	**13 (100.0)**	**0.015**
Non-frail	**16 (22.2)**	**0 (0.0)**	
EAT-10 Score >3*	25 (34.7)	3 (23.1)	0.399
Number of Falls*	1 (1-6)	2 (1-4)	0.573
Urinary Incontinence	30 (41.7)	2 (15.4)	0.057
Fecal Incontinence	**20 (27.8)**	**0 (0.0)**	**0.006**
Pressure Injury	11 (15.3)	2 (15.4)	0.130
Delirium	18 (25.0)	2 (15.4)	0.253
Laboratory findings*			
Hemoglobin (g/dL)	10±2.0	9.6±1.3	0.510
25-OH-vitamin D (ng/mL)	14.4 (3-59.8)	11.1 (3-41.3)	0.616
Creatinine (mg/dL)	**0.98 (0.31-7.62)**	**0.7 (0.23-1.97)**	**0.042**
eGFR (ml/min/1.73 m^2)	57.5 (6-164)	66 (39-128)	0.170
Albumin (gr/dL)	3.0±0.5	2.8±0.8	0.139
C-reactive protein (mg/L)	54.6 (0.6-342)	91.2 (0-233)	0.591
Low-density lipoprotein (mg/dL)	84.5 (27-190)	96.5 (38-129)	0.867

*Values were expressed as mean±standard deviation and median (minimum-maximum). EAT-10: Eating Assessment Tool, eGFR: Estimated glomerular filtration rate, IADL: Instrumental Activities of Daily Living, FRAIL: Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight, ADL: Activities of Daily Living, MNA-SF: Mini Nutritional Assessment-Short Form.

Chronic inflammation increases the formation of reactive oxygen species, leading to oxidative stress. This oxidative stress triggers a vicious cycle that leads to a chronic systemic proinflammatory state, thereby increasing tissue damage[23]. The increase in inflammatory cytokines also leads to reduced skeletal muscle mass and sarcopenia[24]. These changes at the cellular and molecular level result in dysfunction in multiple organ systems, increasing the risk of mortality.

Table III. Cox regression analysis for in-hospital mortality.

	Model 1		Model 2		Model 3	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age (years)	1.01 (0.98-1.05)	0.497	1.01 (0.98-1.05)	0.547	1.01 (0.97-1.05)	0.692
Male Sex	1.48 (0.89-2.49)	0.130	1.48 (0.87-2.53)	0.130	1.49 (0.87-2.56)	0.146
Frailty	3.10 (1.69-5.67)	**<0.001**	3.10 (1.69-5.69)	**<0.001**	2.86 (1.53-5.36)	**0.001**
Cancer			1.02 (0.60-1.74)	0.950	1.04 (0.61-1.78)	0.879
Calf circumference (cm)					1.02 (0.98-1.05)	0.357

CI: Confidence interval. HR: Hazard ratio, model 1: adjusted by sex, age, and frailty; model 2: adds cancer to model 1; model 3: adds calf circumference to model 2.

Frailty, malnutrition, and sarcopenia are closely interrelated geriatric syndromes. Chronic inflammation, mitochondrial dysfunction, and oxidative stress are also involved in the pathogenesis of malnutrition and sarcopenia[25]. Therefore, just like frailty, they are expected to be associated with mortality. In our study, the differences in functional dependence, SARC-F score, and MNA-SF score according to mortality did not reach statistical significance, but this may be related to the fact that patients with malnutrition and sarcopenia were provided supportive treatment.

In the literature, anthropometric measurements, especially calf circumferences, have been among the factors associated with long-term survival in several studies[20,26]. Muscle circumference measurements, which are indicators of muscle mass, are associated with sarcopenia, malnutrition, mobility, and functional dependence[27]. In our study, we found that patients with low calf circumference had higher mortality during in-hospital follow-up.

Creatinine values are related to muscle mass, and low creatinine can be a predictor of mortality in frail, cachectic, and sarcopenic patients[28]. Similarly, our in-hospital mortality data indicated that creatinine level was inversely correlated with mortality in univariate analysis. In the study, which included individuals with high frailty and sarcopenia screening rates, the low creatinine values among non-surviving patients may also be explained by low muscle mass and malnutrition.

The strength of our study is that it is the first to examine the relationship between multiple geriatric syndromes and mortality in older inpatients in our country. There are many studies in the literature investigating the relationship between geriatric syndromes and specific disease groups. However, our study was conducted in a more heterogeneous population, including multiple disease groups.

Nevertheless, our study has some limitations. Firstly, the sample was small and from a single center. Our findings should be supported by multi-center studies with longer follow-up periods.

Conclusions

This study showed that frailty, one of the geriatric syndromes, was an independent risk factor associated with in-hospital mortality, consistent with the literature. Adopting a holistic approach and performing multidimensional geriatric assessment, especially for frail older adults, is essential to increasing patient quality of life and reducing the risk of mortality by preventing frailty.

Informed Consent

Written informed consent was obtained from all study participants.

Ethics Approval

Marmara University Clinical Research Ethics Committee approved the study (Protocol Code: 09.2021.934).

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Authors' Contributions

All authors contributed to the study's conception and design. Material preparation, data collection and analysis were performed by AT, TT and NSD. The first draft of the manuscript was written by TT and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

None.

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