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Associations of Frailty, Defined Using Three Different Instruments, with All-Cause Mortality in a Tertiary Outpatient Clinic in Turkiye

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Purpose: To our knowledge, there have been no comparative studies evaluating the associations of frailty defined using the Tilburg Frailty Indicator (TFI), frailty phenotype by Fried et al, and FRAIL scale with all-cause mortality in Turkiye. In this study, we aimed to evaluate the ability of these instruments in predicting all-cause mortality in outpatients admitted to the outpatient geriatrics clinic of a university hospital.

Patients and Methods: This historical prospective study was performed in the geriatrics outpatient clinic of a university hospital in Istanbul, Turkiye. Consecutive older adults (aged ≥ 70 years) who provided written informed consent were enrolled in the study. The survival status of participants was checked electronically using the official death registry system. Univariate analyses and multivariate Cox regression analyses were performed to determine the independent predictors of mortality.

Results: A total of 198 participants with a median age of 77 years were enrolled. During the median follow-up period of 2236 days, 54 (27.3%) patients died. In univariate analyses, male sex, history of falls in the previous year, dependency in instrumental activities of daily living, malnutrition, and frailty with respect to the phenotype by Fried et al, FRAIL scale, and TFI were associated with mortality. In multivariate Cox regression analyses, frailty according to each of the three frailty instruments, male sex, older age, history of falls, and malnutrition or malnutrition risk were independently associated with mortality. The Fried scale was the best frailty tool among the three frailty instruments used to predict all-cause mortality.

Conclusion: The findings of this study suggest that frailty, determined using each of the three instruments used in the present study, is independently associated with all-cause mortality in patients admitted to the outpatient geriatrics clinic of a university hospital in Turkiye. The Fried scale appears to be the best for predicting all-cause mortality.

Keywords: Turkiye, frailty, mortality, malnutrition, falls, dependency

Introduction

Frailty develops as a result of a cumulative decline in multiple physiological systems, which is mainly due to chronic inflammation, immobility, and disruption of homeostatic reserves.[1,2] Frail subjects have an increased risk of falling, institutionalization in long-term care, hospitalization, disability, and mortality.[3,4]

The prevalence of frailty increases with age regardless of the scale used. Although it varies according to the screening scale used, the prevalence of frailty varies between 4% and 59% and is higher in women.[5] The phenotype of frailty by Fried et al and the FRAIL instrument are widely used to assess physical frailty.[6–8] The Tilburg Frailty Indicator (TFI) is one of the multidimensional frailty instruments that assesses physical, psychological, and social frailty.[9]

Frailty was found to be associated with cardiovascular disease (CVD) morbidity and mortality.[10] It has been shown that pre-frail and frail subjects have higher CVD and mortality risk compared with robust subjects as determined by

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Fried's criteria.[11] Frailty determined by the FRAIL scale and TFI was also associated with an increased risk of mortality.[12,13] In another study, frailty, which was determined by two physical frailty scales (Frailty phenotype, Frailty index) and two multidimensional scales (TFI, Groningen Frailty Indicator), similarly had poor predictive abilities in terms of mortality.[14] In another study conducted among community-dwelling elderly people in China, three physical frailty instruments (Frailty Index, FRAIL, and Frailty phenotype by Fried et al) and TFI were used to assess frailty. All four frailty scales had significant predictive ability in terms of mortality.[15] In two other studies conducted in Brazil and The Netherlands, frailty as determined by TFI was associated with mortality.[13,16] Another recent prospective cohort study conducted in Japan suggests that a multidimensional assessment with respect to frailty provides prognostic information in community-dwelling older adults.[17] In the present study, the main aim was to evaluate the ability of TFI, Frailty phenotype by Fried et al, and FRAIL scale to predict all-cause mortality in outpatients who were admitted to the outpatient geriatrics clinic of a university hospital. To the best of our knowledge, this is the first study to compare the association between these three frailty instruments and all-cause mortality in Turkiye. The secondary aim was to determine factors independently associated with all-cause mortality in the study population.

Methods

Study Design and Participants

We conducted this historical prospective study in the outpatient geriatrics clinic of a university hospital in Istanbul, Turkey. Consecutive older adults (≥70 years of age) who provided written informed consent were enrolled from the outpatient geriatrics clinic of the hospital according to our inclusion and exclusion criteria between January 2015 and February 2016. The exclusion criteria were advanced-stage dementia, cancer, and acute medical or psychological stressful conditions. The survival status of the participants was checked electronically using the official death registry system in March 2021. Data analyses were performed from August to September 2023.

Ethical Statement

The ethical committee of Istanbul University, Istanbul School of Medicine approved the study protocol (no. 2015/1253). The study complies with the Declaration of Helsinki.

Fried Frailty Criteria

The participants were assessed in terms of unintentional weight loss of ≥4.5 kg or ≥5% of body mass in the last year (self-report); weakness (assessment based on the handgrip strength measurement using a Jamar hydraulic hand dynamometer); self-reported exhaustion (have you felt exhausted most of the time during the last week); slow gait speed (<0.8 m/s in four-meter usual gait speed test); and self-reported low physical activity (have you performed less physical activity compared to your peers during the last week). Low handgrip strength was defined as in the study by Fried et al.[6] Individuals were classified as frail for scores 3–5, pre-frail for scores 1–2, and robust for a score of 0.[6]

FRAIL Scale

The FRAIL Scale consists of five components: fatigue, resistance, ambulation, illness, and loss of weight, with scores ranging from 0 to 5 (1 point for each question: frail for scores 3–5, pre-frail for scores 1–2, and robust for a score of 0).[7] The FRAIL scale is used to determine physical frailty. Fatigue is determined by asking how much time during the past 4 weeks the respondent felt tired with responses of "all of the time" or "most of the time" scoring 1 point. Resistance is evaluated by asking if the respondent had any difficulty walking up 10 steps alone without resting and without aids. Ambulation was assessed by asking if the respondent had any difficulty walking several hundred meters alone and without aids. If the respondent had 5 or more illnesses out of 11 total illnesses they score 1 point from this item. Loss of weight was considered if a self-report weight decline of 5% or greater within the past 12 months occurred.[7]

The Tilburg Frailty Indicator (TFI)

The TFI includes 15 self-reported questions. It is a three-dimensional questionnaire used to assess frailty (in physical, psychological, and social domains). The total score ranges from 0 to 15 (with higher scores indicating more severe frailty). Subjects are considered frail if their total score is five or higher.[9] The components of frailty in the TFI are with respect to physical (eight), psychological (four), and social frailty (three). Physical frailty corresponds to physical unhealthiness, weight loss, walking problems, difficulty in maintaining balance, poor hearing, poor vision, lack of strength in the hands and physical tiredness. Psychological frailty corresponds to memory problems, feeling down, feeling nervous or anxious and unable to cope with problems. Social frailty refers to living alone, lack of social relations and lack of social support.[9]

Other Study Variables

We recorded demographic characteristics such as age, gender, marital status, educational status, and monthly income. The Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi) equation was used to estimate glomerular filtration rate (GFR) and was corrected for body surface area to calculate estimated-GFR (e-GFR).[18] Nutritional state was evaluated using the Mini Nutritional Assessment-Short Form (MNA-SF) scale.[19] Dependency in activities of daily living (ADL) and instrumental activities of daily living (IADL) was assessed using the Katz and Lawton scales, respectively.[20,21] History of falls was based on self-report from the participants or their close relatives. Four meter walking test and timed up and go (TUG) test were also performed.[22,23] Survival status was checked electronically from the national registry in Turkey (Death Notification System available at https://obs.saglik.gov.tr).

Statistical Analysis

We used IBM SPSS for Windows version 21 (IBM Corporation, Armonk, NY, USA) for the analyses. We presented categorical data as numbers and percentages and continuous data as means ± standard deviations or medians (interquartile ranges [IQRs]) as needed. We assessed the normality of the distribution of continuous variables using the Kolmogorov–Smirnov test. We used the chi-square test to compare categorical variables, and Student's *t*-test or Mann–Whitney *U*-test for comparison of continuous data. Correlation analyses were performed using Pearson or Spearman tests as needed. A correlation coefficient between 0.3 and <0.5, 0.5 and <0.7, and >0.7 indicated weak, moderate, and strong correlations, respectively.[24] Cox Regression analyses were used to determine the factors associated with mortality. Three separate Cox regression models were used for each frailty scale. Further Cox regression models were planned with respect to the nutritional state and dependency status. Two other models were used to compare the three frailty scales in an unadjusted and adjusted model with respect to their association with all-cause mortality. In these two models, three frailty scales were included in the adjusted and unadjusted models. In all analyses, the statistical significance was set at a two-sided *p*-value of <0.05.

Results

A total of 198 participants (n = 62, 31.3% males) with a median age of 77 (range 70–95, IQR: 9 years) were enrolled. The baseline characteristics of the study population are summarized in Table 1. During a median follow-up of 2236 days (range 233–2553, IQR 118 days), 54 (27.3%) patients died.

The rates of frailty and pre-frailty were 24.3% and 47.6%, respectively, according to Fried criteria. According to the FRAIL criteria, the rates of frailty and pre-frailty were 14.6% and 32.3%, respectively. With respect to the TFI, 47% of the participants were frail. The malnutrition and malnutrition risk rates were 3.1% and 19%, respectively. The rates of dependency in ADL and IADL were 10.6% and 52%, respectively.

The rates of dependency in IADL were higher in patients with frailty than in those without frailty according to the three instruments used (Table 2). The rates of dependency in ADL were also higher in patients with frailty than in those without frailty according to the three instruments used; however, the difference was significant only for patients, with frailty according to the Fried and FRAIL instruments (Table 2).

Table 1 General Characteristics of the Study Population (n = 198)

Variables	N (%)
Sex	
Females	136 (68.7)
Males	62 (31.3)
Marital status	
Married	83 (41.9)
With partner	2 (1)
Single	7 (3.5)
Separated	1 (0.5)
Divorced	3 (1.5)
Widowed	102 (51.5)
Education	
Illiterate	21 (10.7)
Literate	25 (12.8)
First school graduate	76 (38.8)
Secondary school graduate	25 (12.8)
High school graduate	32 (16.4)
College graduate	13 (6.6)
Postgraduate	4 (2)
Unknown	2 (1)
Age (in years), mean ±SD	77.7±5.5
Monthly income (TL)	
< 2000	112 (58.6)
2000–3999	58 (30.4)
4000–5999	16 (8.4)
> 6000	5 (2.6)
Hypertension	156 (81.7)
Diabetes Mellitus	68 (35.6)
Dementia	19 (9.9)
Depression	53 (27.7)
CAD	41 (21.5)

Abbreviations: TL, Turkish liras; CAD, coronary artery disease.

Table 2 Comparison of Dependency Rates Between Frail and Non-Frail Subjects

Variable	Dependent in ADL (%)	P	Dependent in IADL (%)	P
Frail (Fried) (%)	26.7	<0.001	88.9	<0.001
Pre-frail or robust (Fried) (%)	2.9		38.6	
Frail (FRAIL) (%)	31	<0.001	100	<0.001
Pre-frail or robust (FRAIL) (%)	7.1		43.8	
Frail (Tilburg) (%)	14	0.15	65.6	<0.001
Pre-frail or robust (Tilburg) (%)	7.6		40	

Abbreviations: ADL, activities of daily living; IADL, instrumental activities of daily living.

There were weak and insignificant agreements regarding the presence of frailty according to the Fried criteria and FRAIL scale (Kappa = 0.38, p = 0.09), Fried criteria and TFI (Kappa = 0.3, p = 0.08), and FRAIL scale and TFI (Kappa = 0.26, p = 0.09). Likewise, there was weak and insignificant agreement between the Fried criteria and the FRAIL scale in terms of the presence of frailty and pre-frailty (Kappa 0.3, p = 0.06). There were weak-to-moderate correlations

between the scores of Fried, FRAIL, and TFI: between Fried and FRAIL ($r = 0.66$, $p < 0.001$), between FRAIL and TFI ($r = 0.54$, $p < 0.001$), and between Fried and TFI ($r = 0.47$, $p < 0.001$).

There were weak negative correlations between Fried and FRAIL scores and ADL scale scores ($r = -0.34$, $p < 0.001$ and $r = -0.30$, $p < 0.001$). There were weak negative correlations between Fried and FRAIL scores and IADL scale scores ($r = -0.42$, $p < 0.001$ for both). The TFI score was not correlated with the ADL or IADL scale scores ($r = -0.15$, $p = 0.04$ for both). There were weak negative correlations between the Fried, FRAIL, TFI scores and MNA-SF score ($r = -0.40$, $p < 0.001$; $r = -0.44$, $p < 0.001$; and $r = -0.41$, $p < 0.001$, respectively). The physical and psychological subscales of the TFI had weak negative correlations with the MNA-SF scores ($r = -0.36$ and $p < 0.001$ for both). The social subscale of TFI did not correlate with the MNA-SF score ($r = -0.02$, $p = 0.84$).

The mortality rate was significantly higher in males, subjects with a history of falls in the previous year, those with dependency on IADL, those with malnutrition, and those with frailty with respect to Fried, FRAIL, or TFI scores (Table 3) in univariate analyses. Dependency in ADL tended to be associated with mortality, but the association was not significant ($p = 0.09$). The median age, four-meter walking time, and TUG test time were higher in participants who died than in those who survived (Table 3). The median BMI was similar between subjects who died and those who survived (Table 3). The median handgrip strength was similar between the deceased and surviving women. The median handgrip strength was lower in deceased men than in surviving men. Deceased subjects had a lower mean e-GFR than those who survived (Table 3).

Six separate models were used to investigate the association between mortality and the study variables. In multivariate Cox regression analyses, sex, age, history of falls, and frailty according to the Fried criteria (model 1); age, history of falls, and FRAIL criteria (model 2); sex, age, history of falls, and frailty according to the TFI score (model 3); and age and a state of malnutrition or malnutrition risk (model 4) were independently associated with mortality (Table 4).

Table 3 Comparison of Study Variables Between Deceased and Survived Subjects

Variable	Survived	Deceased	P
Males (%) Females (%)	59.7 78.7	40.3 21.3	0.005
Age (median [IQR])	76 (8)	81 (10)	<0.001
A history of falls present (%) No history of falls (%)	56.2 81.7	43.8 18.3	<0.001
Frail (Fried) (%) Pre-frail or robust (Fried) (%)	53.3 79.3	46.7 20.7	0.001
Frail (FRAIL) (%) Pre-frail or robust (FRAIL) (%)	55.2 75.7	44.8 24.3	0.022
Frail (Tilburg) (%) Pre-frail or robust (Tilburg) (%)	62.4 81.9	37.6 18.1	0.002
Malnutrition/malnutrition risk Normal nutritional state	41.9 80.9	58.1 19.1	<0.001
Dependent in ADL (%) Independent in ADL (%)	57.1 74.6	42.9 25.4	0.09
Dependent in IADL (%) Independent in IADL (%)	65 81.1	35 18.9	0.012

(*Continued*)

Table 3 (Continued).

Variable	Survived	Deceased	P
BMI (kg/m^2, median [IQR])	29 (6.90)	29.04 (6.74)	0.77
TUG (kg/m^2, median [IQR])	9 (3)	12 (7.5)	<0.001
Handgrip strength (median [IQR]) males	34 (10)	30 (9)	0.019
Handgrip strength (median [IQR]) females	22 (6)	20 (6)	0.17
4 meter walking time (median [IQR])	4.5 (1.60)	5.6 (2.88)	<0.001
e-GFR (mean ± standard deviation)	76.97 ± 18.92	68.72 ± 18.74	0.01

Abbreviations: IQR, interquartile range; ADL, activities of daily living; IADL, instrumental activities of daily living; BMI, body mass index; TUG, timed up and go test; e-GFR, estimated glomerular filtration rate.

Dependency in ADL or IADL was not independently associated with mortality, and only age and history of falls were independently associated with mortality in Models 5 and 6 (Table 4).

Two additional models were used to compare the three frailty scales with respect to their associations with all-cause mortality (Table 5). In the unadjusted model, only the Fried criteria were independently associated with mortality (p = 0.025), and the TFI tended to have an independent association (p = 0.059). In the adjusted model, only the Fried criteria were independently associated with mortality (p = 0.049). A stepwise Cox model also showed that the Fried scale was the best among the three frailty scales for predicting all-cause mortality (Table 6).

Table 4 Multivariate Cox Regression Analyses Models to Assess the Association of Study Variables with Mortality

Model 1	HR (95% CI)	P
Gender	1.96 (1.03–3.72)	0.041
Age	1.11 (1.05–1.16)	<0.001
History of falls in the last year	2.23 (1.22–4.10)	0.009
e-GFR	1 (0.98–1.02)	0.83
Frailty (Fried criteria)	2.38 (1.28–4.41)	0.006
Model 2		
Gender	1.86 (1.00–3.47)	0.052
Age	1.19 (1.06–1.16)	<0.001
History of falls in the last year	2.38 (1.30–4.34)	0.005
e-GFR	1.00 (0.98–1.02)	0.82
Frailty (FRAIL criteria)	1.44 (0.70–2.95)	0.32
Model 3		
Gender	1.95 (1.04–3.66)	0.036
Age	1.11 (1.06–1.17)	<0.001
History of falls in the last year	2.05 (1.12–3.76)	0.020
e-GFR	1.00 (0.98–1.02)	0.97
Frailty (Tilburg scale)	2.28 (1.20–4.30)	0.011

(*Continued*)

Table 4 (Continued).

Model 4		
Gender	1.81 (0.99–3.32)	0.052
Age	1.11 (1.06–1.17)	<0.001
History of falls in the last year	1.65 (0.87–3.13)	0.125
e-GFR	1.00 (0.98–1.01)	0.74
Malnutrition or malnutrition risk	3.70 (1.97–6.93)	<0.001
Model 5		
Gender	1.78 (0.94–3.38)	0.075
Age	1.11 (1.06–1.17)	<0.001
History of falls in the last year	2.55 (1.40–4.63)	0.002
e-GFR	1.00 (0.98–1.01)	0.74
Dependency in ADL	0.95 (0.39–2.30)	0.91
Model 6		
Gender	2.12 (1.06–4.25)	0.034
Age	1.10 (1.05–1.16)	<0.001
History of falls in the last year	2.40 (1.33–4.35)	0.004
e-GFR	1.00 (0.98–1.02)	0.90
Dependency in IADL	1.46 (0.72–2.98)	0.30

Abbreviations: e-GFR, estimated glomerular filtration rate; ADL, activities of daily living; IADL, instrumental activities of daily living.

Table 5 Multivariate Cox Regression Analyses Models to Compare the Association of Frailty Assessment Tools with Mortality (Adjusted and Unadjusted)

Model 1 (unadjusted)	**HR (95% CI)**	**P**
Frailty (Fried criteria)	2.11 (1.10–4.05)	0.025
Frailty (Tilburg scale)	1.86 (0.98–3.53)	0.059
Frailty (FRAIL criteria)	1.01 (0.47–2.17)	0.99
Model 2 (adjusted)		
Frailty (Fried criteria)	1.97 (1.002–3.87)	0.049
Frailty (Tilburg scale)	1.65 (0.80–3.39)	0.178
Frailty (FRAIL criteria)	0.66 (0.29–1.49)	0.317
Gender	2.01 (1.05–3.85)	0.036
Age	1.11 (1.05–1.17)	<0.001

(*Continued*)

Table 5 (Continued).

History of falls in the last year	1.64 (0.87–3.12)	0.129
e-GFR	1.00 (0.98–1.02)	0.659
Malnutrition or malnutrition risk	3.23 (1.70–6.51)	<0.001

Abbreviation: e-GFR, estimated glomerular filtration rate.

Table 6 Multivariate Stepwise Cox Regression Analyses Models to Compare the Association of Frailty Assessment Tools with Mortality (Adjusted and Unadjusted)

Model 1 (unadjusted)	**HR (Standard Error)**	**P**
Malnutrition or malnutrition risk	3.51 (0.32)	<0.001
Frailty (Fried criteria)	2.23 (0.32)	0.012
Model 2 (adjusted)		
Malnutrition or malnutrition risk	3.47 (0.32)	<0.001
Frailty (Fried criteria)	2.16 (0.32)	0.017
Age	1.11 (0.02)	<0.001
Gender	2.01 (0.32)	0.023
History of falls in the last year	1.68 (0.32)	0.109

Discussion

In this historical prospective study, we investigated the relationship between frailty and all-cause mortality in patients aged ≥70 years admitted to our outpatient geriatrics clinic. We determined frailty status using three commonly used instruments: Fried criteria, FRAIL scale, and TFI.[6,7,9] The median duration of follow-up was more than six years. The rates of frailty were high but significantly varied with respect to the instruments used. In terms of frailty, the agreement between the scales was weak. During the follow-up period, 27.3% of the patients died. Notably, the presence of frailty was independently associated with mortality regardless of the instrument used to determine frailty.

In multivariate Cox regression analyses, frailty and older age were consistently associated with mortality in all models formed in the present study. In an umbrella study which compiled studies involving frailty assessment using Fried's physical frailty phenotype and its modifications; the deficit accumulation frailty index; and FRAIL, frailty was significantly and consistently associated with all-cause mortality.[10] In a mortality study comparing four frailty scales (Frailty Phenotype, Groningen Frailty Indicator, TFI, and Frailty Index), frailty determined by these four scales poorly predicted mortality.[14] In a study conducted in Brazil, the risk of mortality in patients identified as frail by TFI was higher than in those who were not frail.[16] In a study conducted in the Netherlands including 475 patients aged 75 years or older, total score, physical subscale score, and psychological subscale score of the TFI predicted mortality.[13] In a longitudinal study conducted in China using four frailty scales (Frailty Index, Frailty Phenotype, FRAIL, and TFI), all scales except Frailty Phenotype were comparably associated with 4-year hospitalization, and 4- and 7-year mortality. Frailty Phenotype independently predicted only 4- and 7-year mortality (adjusted ORs 1.57 and 2.21, respectively).[15] All four scales poorly predicted 4-year hospitalization in this study. As mentioned in the introduction, two recent studies conducted in Brazil and The Netherlands also showed that frailty assessed with the TFI was associated with mortality.[13,16] In another recent prospective cohort study carried out in Japan, a multidimensional assessment regarding frailty provided prognostic information in community-dwelling older adults.[17]

In the present study, two multivariate Cox regression models (one adjusted and one unadjusted) were used to compare the three frailty scales with respect to their associations with all-cause mortality. In both models, only frailty with respect to the Fried scale was independently associated with all-cause mortality. The results of the stepwise Cox regression model were also in accordance with this finding.

Male sex was independently associated with mortality in the models that included the Fried and TFI scales. The significant relationship between older age, male sex, and mortality was compatible with previous studies.[25,26] It has been reported although the rate of frailty is higher in women than in men, the rate of mortality is higher in frail men than in frail women.[27]

A history of falls was also independently associated with mortality in all three models, including the frailty assessment in the present study. A history fall in the previous year has been shown to be associated with mortality in another retrospective study which was conducted in 2909 patients who were admitted to the hospital for hip fractures at a tertiary university hospital in Spain.[28] In a study conducted on individuals over 50 years of age in Korea, a history of falls was not significantly associated with all-cause death.[29] However, a history of injurious falls was associated with an increased risk of mortality.[29]

In the multivariate Cox regression model including malnutrition assessment, only older age and malnutrition were independently associated with mortality in the present study. In another population-based cohort study performed in Singapore, which included 2804 community-dwelling adults aged 55 years or older at baseline and who were followed up for 12 years, there was a significant association between malnutrition and mortality only in subjects with frailty.[30] However, frailty was associated with mortality even in the absence of malnutrition in that study.[30]

In the present study, the malnutrition and malnutrition risk rates were 3.1% and 19%, respectively. Malnutrition was associated with frailty as defined by Fried, FRAIL, and TFI scores in the present study. In a study conducted in patients with diabetes over the age of 60 years in Mysuru, India, most patients with malnutrition, as evaluated by the MNA, were frail with respect to their TFI scores compared to those without malnutrition (76.5% vs 50%), but the difference was not significant, possibly because of the small sample size.[31]

Univariate analyses showed an association between mortality and dependency in IADL. However, dependency on ADL tended to be associated with mortality, although this relationship was not significant. In another study conducted in China, dependency in either ADL or IADL was associated with mortality.[32] The results suggested that almost all components of the Frailty Index (except chronic diseases) were significant determinants of mortality when examined separately. In the multivariate analyses, frailty and dependency in either ADL or IADL were independently associated with mortality. In another study performed in the Netherlands, dependency on ADL and IADL was significantly associated with mortality.[33]

More than one-tenth of the patients in the present study were dependent in ADL, and more than half of them were dependent in IADL. Frail patients, according to the Fried and FRAIL scores, had significantly higher rates of dependency in ADL and IADL. These findings are consistent with those of previous studies showing that frailty is associated with dependency in ADL and IADL.[34,35] A meta-analysis indicated that frail older adults were more likely to develop dependency in ADL (12 studies, pooled OR = 2.76, 95% CI = 2.23–3.44, $p < 0.00001$; five studies, pooled HR = 2.23, 95% CI = 1.42–3.49, $p < 0.00001$) and IADL (six studies, pooled OR = 3.62, 95% CI = 2.32–5.64, $p < 0.00001$; two studies, pooled HR = 4.24, 95% CI = 0.85–21.28, $p = 0.08$).[36]

Frail patients, according to TFI scores, had higher rates of dependency in ADL and IADL, but the difference was significant only for IADL. The TFI score did not correlate with the ADL or IADL scale scores. In addition, the physical subscale of the TFI did not correlate with ADL or IADL scale scores ($r = -0.19$ and $r = -0.16$, respectively). In another study, only the physical subscale of TFI was correlated with ADL scale score, while both total TFI score and physical subscale score of TFI were correlated with IADL scale score.[37] A 24-month follow-up study conducted in Brazil also suggested that TFI could predict the development of dependency in both ADL and IADL.[16]

In the present study, slow walking pace and poor performance on the TUG test were associated with mortality only in univariate analyses. Low handgrip strength and poor performance in the TUG test have been shown to be associated with short-term mortality.[38] In a study conducted in Japan, TUG test performance was associated with all-cause mortality.[39] It is also reported that slow walking speed is a risk factor for hospitalization, premature death, and falls.[40]

Median handgrip strength was similar between deceased and survived women.

The median handgrip strength was lower in deceased men than in men who survived. A review suggested that handgrip strength was inversely associated with all-cause mortality.[41] In a meta-analysis that included 38 studies, higher levels of handgrip strength were associated with a reduced risk of all-cause mortality (HR, 0.69; 95% CI, 0.64–0.74) compared with lower muscle strength.[42]

In the present study, deceased subjects had a lower mean e-GFR than those who survived. However, we did not observe an independent association between the e-GFR and mortality in the present study. In addition, we did not have data regarding the change in e-GFR during the study period. Further studies with larger sample sizes and longitudinal e-GFR data may provide more information in this regard. In a study conducted in patients aged >75 years, low GFR was significantly associated with mortality.[43] A review in 2014 also suggested a significant relationship between the reduction rate in GFR and mortality.[44]

The rates of frailty and pre-frailty were 24.3% and 47.6%, respectively, according to Fried criteria. According to the FRAIL criteria, the rates of frailty and pre-frailty were 14.6% and 32.3%, respectively. With respect to the TFI, 47% of the participants were classified as frail. Therefore, there was wide variation in the rates of frailty according to these instruments. The rates of frailty and wide variation in the rates of frailty with respect to the different instruments used were in accordance with the rates of frailty reported in previous studies.[14,34,35,45]

A randomized controlled study performed on 424 community-dwelling persons with a mean age of 76.8 suggested that a physical activity intervention for twelve months was associated with improvement in frailty status, especially in participants at higher risk of disability.[46] In another study, thirty-one patients with mild-to-moderate dementia, between 65 and 90 years of age, were included in a six-week aerobic, balance, and combined (aerobic-balance) exercise programs.[47] In that study, all exercise types were associated with improvement in frailty status. In a multicenter study performed in seven European countries, a 12-month structured multimodal intervention program led to a clinically significant improvement in the functional status of nearly a thousand older frail and pre-frail participants with type 2 diabetes mellitus.[48] In another study, in older people with mobility problems over 70 years of age, a six-month patient-centered physical therapy was associated with a significant improvement in frailty.[49] In a study performed in patients with Alzheimer's disease, a six-month home-based and group-based exercise interventions were associated with a significant reduction in the rate of falls and a significantly slower rate of deterioration in terms of frailty compared with those in the control group who received only standard care.[50] A systematic review and meta-analysis of 16 original studies suggested that the existing body of evidence is not sufficient to conclude that interventions in elderly adults is protective against mortality or institutionalization.[51]

The present study provides data on the prognostic value of three commonly and widely used frailty scales. To our knowledge, there are very few studies conducted in Turkiye with respect to the prognostic value of the three frailty instruments used in this study in the outpatient setting. We think that further studies are needed to investigate the prognostic value of such instruments especially in countries like Turkiye. The findings of the present study would encourage researchers to focus on the assessment of frailty in the outpatient setting and investigate the prognostic value of frailty.

The present study has some limitations. First, this was a historical prospective study; therefore, the results may not provide conclusive evidence regarding the association between the study variables and mortality. Second, we only had data on frailty status and other study variables only during the baseline visit. Therefore, significant changes in patients during the study period could not be defined, which may have caused a potential source of confounding. Third, specific causes of mortality were not available; thus, we could not provide data regarding the association of specific causes of mortality, such as cardiovascular death, which has been reported to be associated with frailty. Fourth, the TFI was recently validated in the Turkish population,[52] therefore data with respect to the clinical and prognostic value of the TFI was scarce during the study period. One of the strengths of this study was the relatively long median follow-up period, which was longer than six years. We also obtained the survival data for all participants.

In conclusion, the findings of the present study suggest that frailty as determined either by Fried, FRAIL, or TFI instruments is independently associated with mortality in patients aged 70 years or older who were admitted to a tertiary outpatient geriatrics clinic during a median follow-up duration of more than six years. Malnutrition, as determined by

MNA, was also independently associated with mortality. Furthermore, older age, male sex, and history of falls also seem to be associated with mortality. The findings of this study and previous studies suggest that the assessment of frailty in older patients provides prognostic information. The findings of the present study suggest that the Fried, FRAIL, and Tilburg scales provide significant prognostic information regarding mortality in this population. Comparative analyses suggest that the Fried scale may be better at predicting all-cause mortality than the other two scales used in this study. Further interventional studies are needed to investigate the effects of frailty treatment on mortality.

Data Sharing Statement

The data sets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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