ABSTRACT

**Background:** Frailty is a prevalent geriatric syndrome that can predict mortality in the older people. Aim of this study is to determine if there is an association between frailty and 4-year mortality in the community- dwelling Turkish older people.

**Methods:** The Fried Frailty Index (FFI) and FRAIL scale data from the Kayseri Elderly Health Study (KEHES) were used. Uni- and multivariate analyses were conducted to determine the association between frailty and mortality as assessed by FFI, FRAIL scale.

**Results:** The four-year mortality frequency was found as 7.2% (n=65/905).The gender specific mortality was 2.4% (n=22) in females and 4.8% (n=43) in males. The frequency of mortality in the older people ≥75 years of age was 12.8% (n=34/265) and in those aged 60- 74 years it was 4.8% (n=31/640).The frequency of mortality in the frail, pre-frail, and non-frail older people was 57.4%, 25.9%, and 16.7%, respectively, for the FFI. The corresponding frequency of mortality for the FRAIL scale was 20.6%, 54.0%, and 25.4 %, respectively. In multivariate analysis, male gender (OR 2.67, 95%CI 1.43-4.96) and being frail (OR 5.34, 95%CI 2.45-11.67) were significantly associated with four-year mortality according to the FFI

**Conclusion:** Both the FFI and FRAIL scale may be significant predictors of 4-year mortality in the sample. However, the FFI may be considered as the strongest predictor for 4-year mortality primarily in male gender.

.HZ\RUGV Frailty, Mortality, Older people, Community-dwelling.

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## INTRODUCTION

Turkey's population, like that of most developing countries, is ageing. The older people population of Turkey is more than 6.9 million in 2017. The older people population constitutes about 8.3% of the general Turkish population. In 2013 the older people made up 7.3% of the population in Kayseri/Turkey (the year of our sampling). According to population projections, the proportion of older people is expected to be 10.2% of the general population in 2023 (1). Frailty is a common clinical syndrome in which vulnerability to poor health outcomes such as disability, falls, institutionalization, and mortality is increased (2,3). Frailty prevalence in the community-dwelling older people is reported to be 4.0% - 59.1% in Europe, 21%-44% in Russia, 5%-31% in China, 15% in Mexico and 17%-31% in Brazil (4, 5). In our study that was published in 2014, the frailty prevalence in Kayseri/Turkey was determined as 27.1% and 10.0%, respectively (6). In this study FFI and FRAIL scales were used to assess frailty. FFI determines frailty in five sub-domains: weight loss, exhaustion, low energy expenditure, slowness and weakness (7). The FRAIL scale was initially developed in 2008 by the Geriatric Advisory Panel of the International Academy of Nutrition and Aging (FRAIL:**F**atigue, **R**esistance, **A**mbulation, **I**llness, **L**ow weight) (8).

Frailty is a significant determinant of mortality in the older people. To our knowledge, there are no data showing the relationship between frailty and mortality in the community-dwelling Turkish older people. Numerous valid and reliable scales are available to assess frailty in the older people independent from the causative effects. We designed this study to determine the discriminative power of two frequently used scales; namely the FFI and FRAIL scale, to assess their effectiveness in predicting mortality in the Turkish community-dwelling older people.

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## METHODS

The data of the community-dwelling older people (n=905) who were included in this study were drawn from KEHES. The study group in 2013 was assessed again in 2017 for mortality. KEHES was a cross sectional study in which 1% of the community- dwelling older people (89,303) livings in a city with a population of 1,200,000 were included. Recruitment of community- dwelling older people was done in the August-December 2013 period from 21 Family Health Centers (FHC). Data were collected from the 21 Family Health Care Centers. The distribution of health centers included in the study was stratified according to socio-economic level: low, moderate and good with respect to socio-economic status in the general population. In our initial design for grouping age; we considered grouping as 65-74, 75-84 and older than 85 years was reliable. However in our analysis we changed this grouping as 60-74, ≥75years. The rationale of this new grouping was both relatively low numbers of elderly in some groups (primarily elderly over 80 years and detecting a significant decline after 75 years). Additionally the rationale of including elderly aged 60-64 was their insistent request to be included in the study.

The exclusion criteria are the following: patients who have a prior history of any other cancer, patients who are bedridden and being unwilling to participate in the study. The older people were invited to health own centres and physical examinations were performed. A list of deaths from the last four years- from August 2013 to January 2017-was obtained from the local health authority (Türk Halk Sağlığı Kurumu/ Kayseri). Using this list, a cross match was done with individuals included in the current study to determine the number of deaths in the study

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group.The Medical Ethics Committee of Erciyes University Medical Faculty approved the study (2013/441-02.07.2013).

We used the modified version of the FFI in which physical activity was not included (9, 10). These criteria include four components:

1. Unintentional weight loss of > 4.5 kg (10 lbs) were categorized as positive.
2. Weakness was assessed as grip strength: ≤ 25.6 kg for females and ≤ 14.7 kg for males (≤ 25$^{th}$ percentile) were categorized as positive for the grip strength criterion (≤ 25$^{th}$ percentile =1,≥ 25$^{th}$ percentile=0 ).
3. Exhaustion was assessed by the Geriatric Depression Scale (GDS): ‘‘Do you feel full of energy?’’ (Yes = 0, No = 1) (9- 12).
4. Slowness was assessed by a 4-m walking speed: ≥ 5.67 sec/m for females and ≥ 4.67 sec/m for males (≥ 75$^{th}$ percentile=1, ≤75$^{th}$ percentile=0) was considered as positive for slowness. The older people were categorized as as nonfrail (0 points), prefrail (1 points), and frail (≥2 points).

The FRAIL scale consists of 5 self-reported components—fatigue, resistance, ambulation, illnesses, and loss of weight. The scale score ranges from 0 to 5 points, with 1 point given to each positive answer. Fatigue was evaluated by asking participants if they felt tired most of the time. Resistance was measured by participants' self-report on his/her capacity to climb a flight of stairs. Ambulation was assessed by self-report that they had difficulty in walking several hundred yards alone and without aid disease burden by the presence of 5 or more of a total of 11 diseases as diabetes, heart disease, hypertension, stroke, low iron level (iron deficiency anaemia), osteoporosis, asthma, chronic obstructive pulmonary disease (ie,

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bronchitis/emphysema), anxiety, arthritis/rheumatism, breast cancer, cervical cancer or chronic fatigue syndrome. Weight loss was assessed by 5% or more weight loss within the previous 12 months (13). The older people were categorized as as nonfrail (0 points), prefrail (1 to 2 points), and frail (≥3 points).

The chi-square test was used to compare categorical variables. Binary logistic regression was done for demographic information, socio-economic and smoking status, fear of falling, and having experienced falls. Additionally, both frailty scales were analyzed in logistic regression analysis to determine their sole or combined effect on mortality. Significant variables at $p<0.25$ on univariate analysis were taken into a multiple model and forward stepwise selection was performed using the likelihood ratio statistic at $p<0.10$ stringency level. Odds ratios were also given with 95% confidence intervals. To discriminate the power of the two scales (FFI and FRAIL scale), a chi -square test was performed separately for gender and age groups. R 3.2.0 (www.r-project.org) software was used for statistical analysis. $p<0.05$ was considered statistically significant. Moreover, receiver operating characteristic (ROC) curves were generated to identify the predictive effect of FRAIL and FFI scores on mortality. Area under the ROC curves were calculated with 95% confidence intervals and compared between each other. R 3.2.0 (www.r-project.org ) software and easyROC (14) were used for statistical analysis. p<0.05 was considered statistically significant.

**RESULTS**

We included 905 community-dwelling elderly. However, we failed to calculate frailty in 1.0% (n=8) and 6.0% (n=57) of the elderly for FRAIL and FFI, respectively because of missing data.

Actual numbers of community-dwelling elderly for FFI and FRAIL reduced accordingly and

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new sample size that used to calculate frailty are shown in Table 1-3. In this study the 4-years unadjusted mortality was 7.2% (65/905 older people). The gender specific mortality in males was double that in female4.8% (n=43) and 2.4% (n=22) in males and females, respectively. The 4-years mortality frequency in the older people ≥75 years of age was 12.8% (n=34/265) and in the 60-74 years old group it was 4.8% (n=31/640).

The frequency rates of short period (4-years) mortality in the older people for frail, pre-frail, and non-frail were 57.4%, 25.9%, and 16.7%, respectively, according to the FFI (Table 1). According to the FRAIL scale, the frequency rates of mortality in the frail, pre-frail, and non-frail older people were 20.6%, 54.0%, and 25.4 %, respectively (Table 1). The ratio of nonfrail to frail/prefrail mortality for FFI was 1/16 and 8/29 in female and male respectively. Additionally the ratio of nonfrail to frail/prefrail mortality for FRAIL was 1/21 and 15/26 in female and male respectively (Table 2). In case of determining frailty with the FRAIL scale, the ratio of mortality in the frail/pre-frail compared with the non-frail was more than 21 times and more than 1.5 times higher in females and in males, respectively (Table 2).

A comparison of mortality in the older people aged 60–74 years and ≥75 years yielded significant differences between frailty and mortality as determined by the FFI and FRAIL scale. According to both frailty scales, mortality was higher in the pre-frail group compared with the frail and non-frail in 60–74 years old. In those aged ≥75 years, mortality was significantly high in the frail older people according to the FFI, but the highest mortality frequency was in the pre-frail group according to the FRAIL scale (Table 3).

In addition to determining the effect of frailty on mortality for gender and age, we made a further logistic regression analysis. In univariate logistic regression analysis: age, gender,

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sociodemographic characteristics, falls, fear of falling and the two frailty scales were analyzed (FFI and FRAIL scale) as independent variables for mortality (Table 4). Age ≥75 years and male gender, current smoking, being frail according to the FFI, and being frail or pre-frail according to FRAIL were determined as significant independent variables for mortality. However, in multivariate analysis, male gender (OR 2.67, 95%CI 1.43-4.96) and being frail (OR 5.34, 95%CI 2.45-11.67) were significantly associated with mortality according to the FFI (Table 4).We made further analysis to reveal if any of these measures are superior to each other as well as predicting mortality. Area under the curve (AUC) in ROC analysis was 0.672(0.596-0.747) and 0.588(0.508-0.667) for FFI and FRAIL respectively (Figure 1).

**DISCUSSION**

The primary aim of this study is to determine the four- year mortality frequency according to two different frailty assessment scales in the community-dwelling Turkish older people. This is the first study to provide the association between frailty and mortality in the community-dwelling Turkish older people. The criteria to assess the frailty status were the FFI and FRAIL scale. Both of these frailty scales make an assessment about frailty with relatively different measures. The FFI can be considered as an objective scale, since it has sub-domains reflecting muscle function, such as handgrip and four meters walking speed. Unlike the FFI, the FRAIL scale can be considered as a subjective measure; since its assessment depends on older people self-report. Use of two different scales in the assessment of frailty reinforces our conclusion. On the other hand, deriving our data from an epidemiologic study whose primary aim is not predicting mortality and calculating mortality frequency in a relatively short period may be a weakness of our study.

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Studies that compared the relationship between frailty and mortality for both genders gave different results (increased or decreased) (15-18). We found that frailty is associated with higher mortality that is prominent in male gender (Table 4). Additionally, the FFI showed that the frail/pre-frail and non-frail ratio is a good indicator of mortality in both genders (Table 2). On the other hand, in the case of the FRAIL scale, the highest mortality frequency was prominent in the pre-frail older people. The relatively objective character of the FFI may be the cause of this difference since the subjective character of the FRAIL scale may cause underestimation of frailty. In general, Turkish people over-express their well-being, so the older people in our study that could be grouped in the frail group may have presented themselves as pre-frail (19).

The European Male Aging Study (EMAS) was conducted in relatively young male older people subjects. Two different frailty scales (FFI and FRAIL) were used, as in our study, and a positive relationship was observed between frailty and mortality. In EMAS the hazard ratios (HRs) for mortality were 3.84 and 3.87, respectively, for the FFI and FRAIL scale (20). In a comparison of our study with EMAS we found that there is a positive relationship with frailty and mortality in male gender with the FFI. However, when using the FRAIL scale to assess the relationship between frailty and mortality, our data showed that the frequency of mortality was higher in the pre-frail older people when compared with the frail older people. The reason for the difference between our and the EMAS study may be the relatively low mean age in the EMAS study. Although in the EMAS study both scales showed similar results for frequency of mortality, in our study the FRAIL scale failed to show a similar result. Our explanation for this situation is the underestimation of frailty with a relatively subjective measure (FRAIL scale). Therefore, we may conclude that the FRAIL scale may have variable power as an indicator of frailty in

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different populations. In comparison of FFI and FRAIL for mortality we found that FFI is superior to FRAIL according to ROC analysis.

Indeed we detected several factors related with mortality in univariate analysis.In further analysis we detected two significant factors that are significantly related with increased frequency of mortality. These factors were male gender and being classified as frail according to the FFI scale. Frailty is associated with higher mortality, and the effect of frailty on mortality was strongest in the frail male. In addition, total mortality was higher in males in our study population. The explanation for greater mortality in males could be the higher prevalence of medical comorbidities, such as cardiovascular disease and diabetes mellitus in addition to high smoking frequency, in males.

Increased frequency of mortality over 80 years is well known and the additional positive contribution of frailty over this age is shown in several studies (21-23). Although in univariate analysis increased age was a significant factor for increased mortality, this relationship was not found in multivariate analysis. Additionally, the positive relationship between frailty and mortality in advanced age was not confirmed in multivariate analysis.

**CONCLUSION**

Frailty is a prevalent and substantial geriatric syndrome associated with increased mortality. There are several measures to assess frailty in the older people. Among these, the FFI is the most frequently used and FRAIL is an easy to use scale to assess frailty. In this cross-sectional study we checked the association between frailty and 4-year mortality. The FRAIL scale can be used to assess mortality but our results showed that the FFI is a stronger predictor for mortality than the FRAIL scale.

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**Conflict of interest**

The authors have no conflict of interest to disclose.

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**Table 1**. Age interval, Gender, Income, Living Alone, Smoking Status, Fear of Falling, Falls, FFI and FRAIL scale to assess mortality status
*P*valueforcomparisonbetween "survived" and "died"groups: Chi-square test forcategoricalvariable

| **Variable** | **All (n=905)** | **Survived (n=840)** | **Died (n=65)** | ***p*** |
|---|---|---|---|---|
| **Number(%)** | | | | |
| **Age** | | | | |
| 60-74 | 640(70.7) | 609(72.5) | 31(47.7) | <0.001 |
| 75> | 265(29.3) | 231(27.5) | 34(52.3) | |
| **Gender** | | | | |
| Female | 458(50.6) | 436(51.9) | 22(33.8) | 0.004 |
| Male | 447(49.4) | 404(48.1) | 43(66.2) | |
| **Income** | | | | |
| Low | 192(21.5) | 183(22.1) | 9(13.8) | 0.211 |
| Modarete | 447(50) | 414(49.9) | 33(50.8) | |
| Good | 255(28.5) | 232(28) | 23(35.4) | |
| **LivingAlone** | | | | |
| Maried | 616(68.1) | 571(68) | 45(69.2) | |
| None | 289(31.9) | 269(32) | 20(30.8) | |
| **SmokingStatus** | | | | |
| NeverSmoking | 594(65.6) | 559(66.5) | 35(53.8) | 0.078 |
| FormerSmoker | 80(8.8) | 74(8.8) | 6(9.2) | |
| CurrentSmoking | 231(25.5) | 207(24.6) | 24(36.9) | |
| **Fear of Falling** | | | | |
| Yes | 358(40) | 325(39.2) | 33(50.8) | 0.045 |
| No | 537(60) | 505(49.2) | 32(60.8) | |
| **Falls** | | | | |
| Yes | 216(24.1) | 199(24) | 17(26.2) | 0.365 |
| No | 679(75.9) | 631(76) | 48(73.8) | |
| **FFI** | **All (n=848)** | **Survived (n=794)** | **Died (n=54)** | |
| Frail | 236(27.8) | 205(25.8) | 31(57.4) | <0.001 |
| Pre-Frail | 295(34.8) | 281(35.4) | 14(25.9) | |
| Non-Frail | 317(37.4) | 308(38.8) | 9(16.7) | |
| **FRAIL** | **All (n=897)** | **Survived (n=834)** | **Died (n=63)** | |
| Frail | 90(10) | 77(9.2) | 13(20.6) | 0.001 |
| Pre-Frail | 409(46.6) | 375(45) | 34(54) | |
| Non-Frail | 398(44.4) | 382(45.8) | 16(25.4) | |

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Table 2. Frequency of mortality in female and male according to both FFI and FRAIL scales

| | Female | | | | Male | | | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **All (n=427)** | **Survived (n=410)** | **Died (n=17)** | ***p*** | **All (n=421)** | **Survived (n=384)** | **Died (n=37)** | ***p*** |
| **Number(%)** | | | | | | | | |
| **FFI** | | | | | | | | |
| Frail | 130(30.4) | 117(28.5) | 13(76.5) | <0.001 | 106(25.2) | 88(22.9) | 18(48.6) | 0.001 |
| Pre-Frail | 154(36.1) | 151(36.8) | 3(17.6) | | 141(33.5) | 130(33.9) | 11(29.7) | |
| Non-Frail | 143(33.5) | 142(34.6) | 1(5.9) | | 174(41.3) | 166(43.2) | 8(21.6) | |
| **FRAIL** | **All (n=455)** | **Survived (n=433)** | **Died (n=22)** | | **All (n=442)** | **Survived (n=401)** | **Died (n=41)** | |
| Frail | 66(14.5) | 59(13.6) | 7(31.8) | 0.005 | 24(5.4) | 18(4.5) | 6(14.6) | 0.003 |
| Pre-Frail | 247(54.3) | 233(53.8) | 14(63.6) | | 162(36.7) | 142(35.4) | 20(48.8) | |
| Non-Frail | 142(31.2) | 141(32.6) | 1(4.5) | | 256(57.9) | 241(60.1) | 15(36.6) | |

*P* valueforcomparisonbetween "survived" and "died"groups: Chi-square test forcategoricalvariable

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Table 3. Frequency of mortality in 60-74 years old and >75 years old according to both FFI and FRAIL scales

| | 60-74 years | | | | 75>years | | | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **All (n=609)** | **Survived (n=581)** | **Died (n=28)** | ***p*** | **All (n=239)** | **Survived (n=213)** | **Died (n=26)** | ***p*** |
| **Number(%)** | | | | | | | | |
| **FFI** | | | | | | | | |
| Frail | 128(21) | 117(20.1) | 11(29.3) | 0.038 | 108(45.2) | 88(41.3) | 20(76.9) | 0.002 |
| Pre-Frail | 230(37.8) | 220(37.9) | 10(35.7) | | 65(27.2) | 61(28.6) | 4(15.4) | |
| Non-Frail | 251(41.2) | 244(42) | 7(25) | | 66(27.6) | 64(30) | 2(7.7) | |
| | **All (n=634)** | **Survived (n=604)** | **Died (n=30)** | ***p*** | **All (n=263)** | **Survived (n=230)** | **Died (n=33)** | ***p*** |
| **FRAIL** | | | | | | | | |
| Frail | 51(8) | 46(7.6) | 5(16.7) | 0.123 | 39(14.8) | 31(13.5) | 8(24.2) | 0.010 |
| Pre-Frail | 295(46.5) | 280(46.4) | 15(50) | | 114(43.3) | 95(41.3) | 19(57.6) | |
| Non-Frail | 288(45.4) | 278(46) | 10(33.3) | | 110(41.8) | 104(45.2) | 6(18.2) | |

*P* valueforcomparisonbetween "survived" and "died"groups: Chi-square test forcategoricalvariable

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Table 4. UnivariateandMultivariateanalysistoassesstomortalitywith Age interval, Gender, Income, LivingAlone, SmokingStatus, Fear of Falling ,Falls, FFI and FRAIL scale

| Variable | Univariate | | Multivariate | |
|---|---|---|---|---|
| | Odds(95%CI) | $p^*$ | Odds(95%CI) | $p^{**}$ |
| **Number(%)** | | | | |
| **Age** | | | | |
| 60-74 | 1.00 | - | - | - |
| 75> | 2.89(1.74-4.82) | <0.001 | - | - |
| **Gender** | | | | |
| Female | 1.00 | - | 1.00 | - |
| Male | 2.11(1.24-3.59) | 0.006 | 2.67(1.43-4.96) | 0.002 |
| **Income** | | | | |
| Good | 1.00 | - | - | - |
| Modarete | 1.62(0.76-3.46) | 0.211 | - | - |
| Low | 2.02(0.91-4.46) | 0.084 | - | - |
| **LivingAlone** | | | | |
| None | 1.00 | - | - | - |
| Maried | 0.94(0.55-1.63) | 0.834 | - | - |
| **SmokingStatus** | | | | |
| NeverSmoking | 1.00 | - | - | - |
| FormerSmoker | 1.30(0.53-3.18) | 0.573 | - | - |
| CurrentSmoking | 1.85(1.08-3.19) | 0.026 | - | - |
| **Fear of Falling** | | | | |
| No | 1.00 | - | - | - |
| Yes | 1.60(0.97-2.65) | 0.068 | - | - |
| **Falls** | | | | |
| No | 1.00 | - | - | - |
| Yes | 1.13(0.63-2.00) | 0.680 | - | - |
| **FFI** | | | | |
| Non-Frail | 1.00 | - | 1.00 | - |
| Pre-Frail | 1.71(0.73-4.40) | 0.220 | 1.82(0.77-4.29) | 0.172 |
| Frail | 5.18(2.41-11.09) | <0.001 | 5.34(2.45-11.67) | <0.001 |
| **FRAIL** | | | | |
| Non-Frail | 1.00 | - | - | - |
| Pre-Frail | 2.17(1.18-3.99) | 0.013 | - | - |
| Frail | 4.03(1.86-8.72) | <0.001 | - | - |

$p^*$valueforcomparisonbetween "survived" and "died"groups: UnivariateLogisticRegression test variable. $p^{**}$valueforcomparisonbetween "survived" and "died"groups: MultivariateLogisticRegression test variable.

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