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Original Article

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Frailty and Dependency in Kidney Transplant Candidates

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ABSTRACT

Objective: Frailty is very common in kidney disease, and most of the end-stage kidney disease patients are described as frail. This study aimed to define frailty condition in kidney transplant candidates and investigate its relationship between dependency and laboratory parameters.
Methods: One hundred two end-stage kidney disease patients on deceased kidney transplant waiting list were included in the study. Modified Fried Frailty Index and FRAIL frailty questionnaire were used to assess frailty and Activities of Daily Living scale and Instrumental Activities of Daily Living scale to assess functional dependency in kidney transplant candidates.
Results: The patients' mean age was 49.09 ± 13.77 years. According to the Modified Fried Frailty Index, 30.4% of patients were non-frail, 48.0% were pre-frail, and 21.6% were frail. According to the FRAIL scale, 34.3% of patients were non-frail, 40.2% were pre-frail, and 25.5% were frail. C-reactive protein level was found to be higher in frail and pre-frail patients ($P = .049$; $P = .010$). Frailty increased with age. According to the Activities of Daily Living scale 15 (14.7%) of the patients and according to the Instrumental Activities of Daily Living scale 27 (26.5%) of the patients were dependent. It was observed that frail patients were more dependent on Activities of Daily Living scale and Instrumental Activities of Daily Living scale ($P < .001$). Multivariate regression analyses revealed C-reactive protein and Activities of Daily Living scale are independent predictors of frailty.
Conclusion: In our study, we found that frailty increased with age, with C-reactive protein levels as a marker of inflammation, and it had a negative impact on the Activities of Daily Living scale affecting daily life to a statistically significant degree.
Keywords: Frailty, functional dependency, inflammation, kidney transplant candidates

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INTRODUCTION

Frailty is characterized by decreased physiological function, endurance, and strength. It increases the participants' vulnerability to functional dependency and/or mortality.[1] There are various definitions and numerous criteria in the literature on frailty. Whichever definition of frailty is used, it has been shown to predict negative outcomes such as falls, hospitalization, poor quality of life, and death in the general population.[2] Recently, the increased frailty prevalence and vulnerability to stress in patients with kidney disease have drawn the attention of transplant physicians, nephrologists, and kidney health professionals.[3] As in the general population, frail patients with kidney disease have been shown to be at a high risk for morbidity and mortality.[4,5] Frailty is prevalent in kidney diseases, and most of the patients with end-stage kidney disease (ESKD) are described as frail.[6] Frailty has also a significant impact on the transplantation probability. The probability of transplantation decreases in the severely frail patients and frail patients on the waiting list are more likely to die or to be removed from the waiting list compared

to non-frail patients.[7,8] Furthermore, frail patients are twice as likely to develop delayed graft function and are at a higher risk of prolonged or recurrent hospitalization after transplantation.[9] Consequently, frail patients experience higher mortality and adverse outcomes after transplantation compared to non-frail patients.[10]

Identifying frail patients and adopting a multidisciplinary approach to correct frailty may provide benefit to the patients and healthcare professionals in terms of increased morbidity and mortality caused by frailty. In our study, we aimed to detect the frailty rate in our kidney transplant candidates on the waiting list using Modified Fried Frailty Index (FFI) and FRAIL frailty questionnaire and to evaluate the association between frailty, functional dependency, laboratory, and clinical parameters.

METHODS

This was a cross-sectional observational study. One hundred two kidney transplant candidates over 18 years and able to respond to questionnaires were included. The study population was selected from patients on kidney transplant waiting list followed up at the Organ Transplantation Evaluation clinic between September 2020 and May 2021. Demographic data including age, gender, body mass index, education level, smoking habit, primary kidney disease, dialysis duration, dialysis type, transplant history, and current comorbidities were recorded. Laboratory data including complete blood count, glucose, c-reactive protein (CRP), serum creatinine, blood urea nitrogen (BUN), albumin, alanine and aspartate transaminase, phosphorus, calcium, parathyroid hormone, 25-OH vitamin D, interleukin-6, LDL cholesterol, HDL cholesterol, and triglyceride were recorded at the time of routine outpatient clinic follow-up.

The frailty status is determined using both the Modified FFI and the FRAIL frailty questionnaire, both of which have been validated in chronic kidney disease (CKD), elderly, and transplant populations.[11] Questionnaire forms were completed through face-to-face interviews with the patients during their planned clinic visits.

The Modified Fried frailty phenotype assesses frailty in 5 domains: unintentional weight loss (in last 12 months) >4.5 kg was categorized as positive (1 point), weakness was assessed as the grip strength: ≤16 kg for females and ≤27 kg for males were categorized as positive for the grip strength criterion (1 point), exhaustion was assessed by the Geriatric Depression Scale: "Do you feel lack of energy?" (if yes 1 point), slowness was assessed by the 4 m walking speed <0.8 m/s (if yes 1 point), and limitation of physical activity (if yes 1 point). Scores range from 0 to 5 and are classified as non-frail (0 points), pre-frail (1-2 points), and frail (≥3 points).[1,12]

According to Modified FFI, the cutoff low muscle strength by handgrip, which can be used to identify probable sarcopenia, is 16 kg in females and 27 kg in males.[13] The cutoff points in the Turkish population are 20 kg in females and 35 kg in males.[14]

The FRAIL frailty questionnaire was created and validated by a comprehensive systematic review of existing frailty scales by the International Academy of Nutrition and Aging task force (IANA).[15,16] 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. Patients were categorized as non-frail (point 0), pre-frail, (points 1-2), and frail (points ≥3).[17]

For the evaluation of functional dependency status, Activities of Daily Living (ADL) and Instrumental Activity of Daily Living (IADL) questionnaires were used. The ADL includes 6 items: dressing, eating, bathing, continence, using the toilet, and getting out of bed or chair. Individuals are defined as positive when they report that they have difficulty in any item of the ADL, are unable to fulfill the task, or that they receive help from another person to perform the task.[18]

The IADL includes 8 items: shopping, preparing meals, managing money, using the telephone, doing laundry, doing housework, traveling, and administering medication. It is defined as positive, if the respondent reports difficulty in performing that task.[19]

This study conforms with the principles outlined in the Declaration of Helsinki and the design was approved by the institutional review board of Marmara University Hospital. All participants gave written informed consent (Protocol number: 12.06.2020.649).

Statistical Analyses

The statistical program Statistical Package for Social Sciences (SPSS) version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) was used for the statistical analysis. Categorical variables were compared

MAIN POINTS

- Frailty is very common in kidney disease, and most of end-stage kidney disease patients are described as frail.
- In our study, we aimed to detect frailty rate in our kidney transplant candidates on waiting list using Modified Fried Frailty Index and FRAIL Frailty questionnaire, and to evaluate association between frailty, functional dependency, laboratory and clinical parameters.
- We found that frailty increased with age, with C-reactive protein levels as a marker of inflammation, and it had a negative impact on the Activities of Daily Living scale affecting daily life to statistically significant degree.
- Screening frailty and functional dependence along with the inflammation parameters is crucial in waitlisted end stage kidney disease patients.
- Initiating special rehabilitation programs, nutritional support, and exercise intervention to improve frailty may lead to an increase in the long-term quality of life and survival of wait-listed patients.

with the Chi-square test. "Kolmogorov–Smirnov analysis was performed to determine whether the continuous variables were normally distributed. Normally distributed continuous variables were compared with the independent sample *t*-test, and those that did not show normal distribution were compared with the Mann–Whitney *U* test." One-way analysis variance (one-way variance) test was used to compare 3 groups according to the modified frail score. Pearson correlation analysis was used to evaluate intergroup relations. Independent markers of frailty were determined using binary logistic regression analysis. The parameters which were found to be statistically significant between frail and other groups (healthy and pre-frail groups) were put into the multivariate regression analysis model. A *P*-value of <.05 was accepted for statistical significance.

RESULTS

One hundred two patients were included. Patients' mean age was 49.09 ± 13.77 years and 48 (47.1%) of the patients were female. The number of patients receiving hemodialysis was 67 (65.7%) and peritoneal dialysis was 12 (11.8%). The number of patients with stage 5 CKD but had not yet been started on dialysis was 23 (22.5%).

The patients were grouped according to Modified FFI as non-frail, pre-frail, and frail. Thirty-one (30.4%) of the patients were non-frail, 49 (48.0%) were pre-frail, and 22 (21.6%) were frail. According to the FRAIL questionnaire, 35 (34.3%) of the participants were non-frail, 41 (40.2%) were pre-frail, and 26 (25.5%) were frail. The level of dependence in performing activities of daily living and instrumental activities of daily living was found in 15 (14.7%) patients according to the ADL scale and 27 (26.5%) according to the IADL scale. According to Modified FFI (cutoff <16 kg in females and <27 kg in males) 11 (10.8%) female and 17 (16.7%) male had low muscle strength by handgrip, which can be used to identify possible sarcopenia. According the cut-off points in the Turkish population (cutoff <20 kg in females and <35 kg in males), 25 (24.5%) female and 37 (36.3%) male hadlow muscle strength by handgrip. Frailty and dependency data of patients are shown in Table 1.

Non-frail patients according to Modified FFI were younger than the pre-frail (42.16 ± 13.86 vs. 51.39 ± 13.52 years, *P* = .010) and frail patients (42.16 ± 13.86 vs. 51.45 ± 10.91 years, *P* = .049). The CRP level of the frail patients was found to be higher than the non-frail (19.89 ± 19.32 vs. 6.89 ± 6.39 mg/dL, *P* = .002) and pre-frail patients (19.89 ± 19.32 vs. 9.92 ± 11.61 mg/dL, *P* = .011).

The comparison of laboratory and demographic parameters of patients according to Modified FFI is shown in Tables 2 and 3.

It was observed that the patients who were frail according to Modified FFI were more dependent on the ADL and IADL scales (*P* < .001) (Figure 1). Multivariate regression analyses revealed that CRP and ADL scales werer independent predictors of frailty (Table 4). When the parameters including gender, diabetes, vitamin D levels, and interleukin-6, which were found to have a *P*-value less than 0.10 between frail and other groups (healthy and pre-frail groups), were put into the multivariate regression analysis model, we did not find a statistical significance on frailty and the significance of the parameters including age, CRP, and activities of daily living that we found significant before also decreased.

Table 1. Frailty and Dependency Data of Patients

Parameter	All Patients (n = 102)
Modified FFI, n (%)	
Non-frail	31 (30.4%)
Pre-frail	49 (48.0%)
Frail	22 (21.6%)
FRAIL Frailty Questionnaire, n (%)	
Non-frail	35 (34.3%)
Pre-frail	41 (40.2%)
Frail	26 (25.5%)
Dependent according to ADL scale, n (%)	15 (14.7%)
Dependent according to IADL scale, n (%)	27 (26.5%)
Low muscle strength by hand grip, n (%)	
According to Modified FFI cutoff points	
Female <16 kg	11 (10.8%)
Male <27 kg	17 (16.7%)
According to Turkish population cutoff points	
Female <20 kg	25 (24.5%)
Male <35 kg	37 (36.3%)

ADL, activity of daily living; FFI, fried frailty index; IADL, instrumental activity of daily living.

In the correlation analysis, positive correlation was found between Modified FFI and FRAIL Frailty Questionnaire (r = .649, $P < .001$). A negative correlation was found between the Modified FFI and the ADL scale ($r = -0.353$, $P < .001$) and the IADL scale ($r = -0.429$, $P < .001$).

DISCUSSION

In the present study, we demonstrated that frailty is common in kidney transplant candidates and increases with age. Frailty is associated with high CRP levels and it had a negative impact on ADL scale affecting daily life. A significant correlation was found between age and frailty. C-reactive protein and ADL scale are independent predictors of frailty. Also, a significant correlation was found between FRAIL questionnaire and Modified FFI.

In the CKD population, most studies have defined frailty using the Modified FFI.[4] Since frailty results of the Modified FFI and FRAIL questionnaire were similar according to our study, 2 tools

Table 2. The Comparison of Demographic Data of the Patients According to Modified Fried Frailty Index

Parameter	All Patients (n = 102)	Non-Frail (n = 31)	Pre-Frail (n = 49)	Frail (n = 22)	*P*
Age, years	49.09 ± 13.77	42.16 ± 13.86	51.39 ± 13.52	51.45 ± 10.91	***.010** **#.049**
Sex, n (%)					
Female	48 (47.1%)	13 (41.9%)	25 (51.0%)	10 (45.5%)	.832
Male	54 (52.9%)	18 (58.1%)	24 (49.0%)	12 (54.5%)	
Body mass index, kg/m^2	26.35 ± 5.63	25.10±5.07	27.49±6.24	25.58±5.05	.16
Education, n (%)					
Primary school	47 (46.1%)	12 (38.7%)	23 (46.9%)	11 (50.0%)	.738
Middle school	9 (8.8%)	2 (6.5%)	6 (12.2%)	2 (9.1%)	
High school	27 (26.5%)	10 (32.3%)	10 (20.4%)	5 (22.7%)	
University	10 (9.8%)	3 (9.7%)	7 (14.3%)	1 (4.5%)	
Iliterate	9 (8.8%)	4 (12.9%)	3 (6.1%)	3 (13.6%)	
Cause of primary kidney disease, n (%)					
Diabetes mellitus	20 (19.6%)	3(9.7%)	10 (20.4%)	7 (31.8%)	.444
Hypertension	15 (14.7%)	4 (12.9%)	7 (14.3%)	4 (18.2%)	
Glomerular disease	29 (28.4%)	9 (29.0%)	15 (30.6%)	5 (22.7%)	
Unknown	9 (8.8%)	4 (12.9%)	4 (8.2%)	1 (4.5%)	
Others	29 (28.4%)	10 (32.3%)	14 (28.6%)	5 (22.7%)	
Dialysis time, months	30.22 ± 43.35	28.17 ± 41.76	28.95 ± 45.74	29.81 ± 41.37	.991
Dialysis type, n (%)					
Hemodialysis	67 (65.7%)	17 (54.8%)	32 (65.3%)	18 (81.8%)	.88
Peritoneal dialysis	12 (11.8%)	4 (12.9%)	6 (12.2%)	2 (9.1%)	
Transplant history, n(%)					
Yes	10 (9.8%)	2 (6.5%)	5 (10.2%)	3 (13.6%)	.633
No	92 (90.2%)	29 (93.5%)	44 (89.8%)	19 (86.4%)	
Comorbidity, n (%)					
Hypertension	72 (70.6%)	18 (58.1%)	37 (75.5%)	17 (77.3%)	.107
Diabetes mellitus	30 (29.4%)	5 (16.1%)	15 (30.6%)	10 (45.5%)	.095
Coronary artery disease	19 (18.6%)	4 (12.9%)	10 (20.4%)	5 (22.7%)	.557
Heart failure	4 (3.9%)	1 (3.2%)	2 (4.1%)	1 (4.5%)	.946
COPD	3 (2.9%)	0 (0.0%)	2 (4.1%)	1 (4.5%)	.497

COPD, chronic obstructive pulmonary disease; SLE, systemic lupus erythematosus.
*Comparison between the healthy and pre-frail groups; #comparison between healthy and frail groups; ¶comparison between pre-frail and frail groups.

may be used for screening frailty in kidney waitlist patients. Furthermore, if the measurement of the handgrip is unable, FRAIL questionnaire, which does not require measurement in practice or in the outpatient clinic, can be used.

Frailty is common in advanced CKD patients. Its prevalence ranges from 15% to 21% depending on which criteria and classification are used and is more frequent than in the general population, with reported rates of 3%-6%.[4] A lower rate of frailty is seen in waitlisted patients compared to hemodialysis patients.[20] In the study conducted by Haugen et al in which 4552 kidney transplant candidates were included, the frailty status of the patients was determined according to the Fried phenotype, and 12% of the patients were found frail.[21] In the study by Fernandez et al,[22] 18.1% of the patients were identified as frail among 2089 kidney transplant candidates. Worthen et al[23] evaluated frailty in 542 kidney transplant candidates who were on the waiting list, according to the Frailty phenotype,

Table 3. The Comparison of Laboratory Parameters of the Patients According to the Modified Fried Frailty Index

Parameter	All Patients (n = 102)	Non-frail (n = 31)	Pre-frail (n = 49)	Frail (n = 22)	*P*
Glucose (mg/dL)	109.32 ± 58.76	113.37 ± 89.88	109.74 ± 41.81	109.05 ± 36.47	.958
Blood urea nitrogen (mg/dL)	52.3 ± 19.59	54.03 ± 18.78	54.79 ± 20.68	43.95 ± 18.32	.105
Creatinine (mg/dL)	6.73 ± 1.91	6.65 ± 1.75	6.83 ± 1.97	6.13 ± 1.76	.369
AST (U/L)	13.96 ± 6.30	12.92 ± 4.53	14.25 ± 7.40	14.35 ± 6.30	.630
ALT (U/L)	14.09 ± 8.12	13.00 ± 5.63	14.69 ± 10.00	13.64 ± 6.84	.669
LDL (mg/dL)	107.78 ± 51.64	116.50 ± 69.58	100.79 ± 40.44	111.74 ± 49.59	.427
HDL (mg/dL)	45.05 ± 12.48	42.71 ± 10.45	45.13 ± 13.65	47.55 ± 13.25	.429
Triglyceride (mg/dL)	163.02 ± 83.31	168.20 ± 87.00	164.78 ± 90.03	152.36 ± 61.78	.806
Albumin (g/dL)	4.19 ± 0.47	4.24 ± 0.57	4.21 ± 0.45	4.06 ± 0.40	.412
Calcium (mg/dL)	9.1 ± 0.75	8.78±0.74	9.18±0.72	9.25±0.60	.056
Phosphorus (mg/dL)	4.80 ± 1.35	4.75 ± 1.08	4.93 ± 1.54	4.45 ± 1.27	.415
Parathyroid hormone (ng/L)	387.01 ± 344.96	360.67 ± 293.26	372.40 ± 320.70	428.04 ± 469.14	.783
25 (OH) Vitamin D (µg/L)	16.75 ± 13.58	20.29 ± 16.93	16.41 ± 12.08	11.26 ± 10.13	.090
Leukocyte (x10^3/µL)	7.31 ± 2.02	7.32±2.06	7.17 ± 2.02	7.62 ± 2.19	.714
Neutrophil (x10^3/ µL)	4.68 ± 1.54	4.71±1.74	4.46 ± 1.43	5.02 ± 1.51	.404
Lymphocyte (×10^3/ µL)	1.77 ± 0.73	1.72 ± 0.53	1.86 ± 0.81	1.68 ± 0.86	.566
Hemoglobin (g/dL)	11.55 ± 1.64	11.92 ± 1.36	11.52 ±1.71	10.96 ± 1.83	.135
Platelet (×10^3/ µL)	224.39 ± 74.01	228.73 ± 72.82	221.27±85.4	220.40 ± 50.91	,897
C-reactive protein (mg/L)	10.91 ± 13.00	6.89 ± 6.39	9.92 ± 11.61	19.89±19.32	**#.002** **¶.011**
Interleukin-6 (pg/mL)	10.85 ± 13.76	6.16 ± 4.06	12.68 ± 17.15	15.16 ± 15.19	.078
Fibrinogen (mg/dL)	491.1 ± 123.4	482.3 ± 136.4	478.8 ± 113.2	540.9 ± 131.1	.188

Data presented as mean ± SD.
*Comparison between the healthy and pre-frail groups; #comparison between healthy and frail groups; ¶comparison between pre-frail and frail groups.
Bold values in the tables indicate that the analysis is statistically significant.

frailty index, and clinical frailty scale, the prevalence of frailty was found to be 16%. In these studies, the authors showed only the prevalence of frail patients and there were not enough data for the pre-fail patients. McAdams-DeMarco et al[24] evaluated the frailty with the Fried phenotype in 1975 ESRD patients aged ≥18 years and were evaluated for kidney transplantation and found that 18.4% of patients were frail, 62.7% were pre-frail, and 18.8% were non-frail. Similarly, we showed that almost two-third of our patients were classified as pre-frail or frail according to Modified FFI and FRAIL Frailty Questionnaire. In our study, the mean age of non-frail, pre-frail, and frail patients was 42.16 ± 13.86; 51.39 ± 13.52, and 51.45 ± 10.91 years, respectively. It was found that frailty increases with age in kidney transplant candidates, which is consistent with previous studies.[20,25]

Malnutrition is very common in patients with CKD and progressively increases across stages of CKD.[26] The progress of kidney disease causes decreased food intake and appetite. The restriction of diet contributes to malnutrition, sarcopenia, and also frailty in CKD patients.[27] Furthermore, oxidative stress increases in CKD stage 5 and may beassociated with frailty and sarcopenia.[28] Low muscle strength by handgrip can be used to identify probable sarcopenia. According to Modified FFI, 10.8% of female and 16.7% of male have low muscle strength by hand grip; according to the cutoff points in the Turkish population, 24.5% of female and 36.3% of male have low muscle strength by handgrip in our study. If we do not use our own Turkish cut-off points, we are actually missing probable sarcopenic patients which is important for patients' morbidity and mortality. We should keep in mind different cutoff points of countries when identifying probable sarcopenia.

It is known that CKD and beyond that, in Stage 5 CKD on dialysis, inflammation increases without any other underlying infection or inflammatory disease and is an important risk factor for mortality, especially in ESKD.[29-32] The presence of inflammation has also been associated with increased mortality in kidney transplant candidates who are on the waiting list.[33] McAdams-DeMarco et al[24] showed an association between frailty and increased inflammation (IL-6, CRP, soluble tumor necrosis

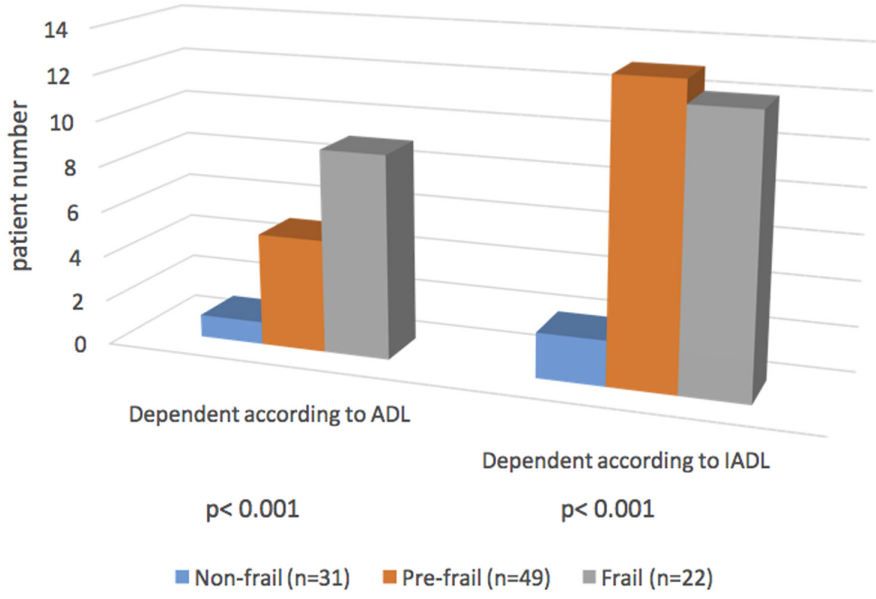

Figure 1. The association between frailty (according to Modified Fried Frailty Index) and dependency.
ADL, activity of daily living; IADL, instrumental activity of daily living.

factor receptor-1) in ESKD patients on kidney transplant waiting list. The authors suggest that inflammatory markers should be measured along with frailty status during the evaluation of transplant candidates. In our study, the mean CRP value in frail transplant candidates was 19.89 mg/L, and it was found to be significantly associated with frailty (P = .028). In a study by Haugen et al,[33] frailty–inflammatory index, which combines inflammatory indicators such as CRP, IL-6, and tumor necrosis factor-alpha with Fried's criteria was defined and they revealed that IL-6 has been determined as a predictor for the mortality in 1154 kidney transplant candidates. The researchers argued that measuring IL-6 in frail transplant candidates could help detect patients at risk and identify those who would benefit from exercise interventions such as rehabilitation.[33] In our study, no significant relationship was found between IL-6 and frailty. This can be explained by small sample size and cross-sectional nature.

Functional independence is a parameter that reflects the ability to take care of oneself.[3] It has been shown to lead to poor outcomes, including death, in ESKD patients, regardless of age.[34,35] In the course of CKD, reaching stage 5 and starting dialysis treatment is associated with a transition from independence to dependence, irrespective of age. About 50% of patients on dialysis were functionally dependent.[36,37] Chu et al[38] evaluated 3168 ESKD patients aged ≥18 years at the time of kidney transplant evaluation in terms of functional independence with the ADL and IADL scales. In this study, functional dependence was found in 7.5% of the patients according to the ADL scale and in 31.5% of the patients according to the IADL scale. In our study, 13.7% of patients were dependent according to ADL scale and 26.5% were dependent according to IADL scale. Functional dependence was found in frail individuals at 40.1% according to the ADL scale and at 54.5% according to the IADL scale. Although higher frailty rates were reported in our study population, the functional dependence rate was found to be similar to the above study.

Table 4. Multivariate Logistic Regression Analyses for Frailty in Kidney Transplant Waiting List

Variable	Exp (B) (%95 CI)	*P*
Age	0.988 (0.937–1.042)	.652
C-reactive protein	1.053 (1.006–1.102)	**.028**
Activities of daily living	0.209 (0.057–0.771)	**.019**

In our study, as seen in other studies, frailty is common in kidney transplant candidates. It can be accepted that the general health status of the patients who are placed on the kidney transplant waiting list is better than patients who are not eligible to be transplanted. On the other hand, previous studies reported that among patients who were waitlisted for kidney transplantation, considered to be healthy enough to undergo kidney transplantation following a thorough evaluation, about 20% met the frailty criteria.[10] Patients with CKD stage 5 are evaluated for kidney transplantation in accordance with KDIGO guidelines and a detailed evaluation is performed based on comorbidities. Although frailty has not yet been included in the guidelines as a part of evaluation, it is associated with poor outcomes such as delayed graft function, delirium, early hospitalization, more-extended hospitalization, poor health-related quality of life, immunosuppression intolerance, and death after kidney transplantation.[9,10,39-43] Frailty can be considered a potentially modifiable parameter and corrected prior to kidney transplant in contrast to

non-modifiable factors such as age, gender, or race.[44] It is crucial to identify frail patients who can benefit from rehabilitation, to exercise programs before transplantation, and to increase their physiological reserves while waiting for kidney transplantation.

Although frailty is a geriatric syndrome caused by a decrease in the individual's response to stress factors, our study showed that frailty is common in relatively younger ESKD patients. It is well known that frailty is associated with increased falls, long-term hospitalization, sarcopenia, delirium, and even mortality.[45] Indeed, ADL scale is a predictor of frailty according to our findings. It may be explained by association between sarcopenia and frailty. On the other hand, dependency and frailty are closely related since the incidence of dependency is increased in frail patients and frailty occurs in dependent patients.

The major limitations of our study are the small sample size and the lack of a control group who were deemed unsuitable to be placed on the transplant waiting list. Furthermore, we did not evaluate vascular access which might contribute to frailty. It is well known that gender, diabetes, vitamin D levels, and interleukin-6 parameters can also affect frailty. These parameters were found to have a *P*-value less than .10 in our cohort. When we have included these parameters into the multivariate analysis, we did not find a statistical significance on frailty and the significance of the parameters including age, CRP, and activities of daily living that we found significant before also decreased. Since the number of our patients is relatively low, we think that the increase in the number of parameters added to the multivariate analysis decreases statistical significance.

CONCLUSIONS

In conclusion, screening frailty and functional dependence along with inflammation parameters is crucial in waitlisted ESKD patients.

Ethics Committee Approval: The study protocol was approved by the institutional review board of Marmara University Hospital (Date: 12.06.2020, Protocol number: 12.06.2020.649).

Informed Consent: Informed consent was obtained from all patients included in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.R., D.B.A., S.T.; Design – A.R., D.B.A., C.Ş.T., A.T., A.V., S.T.; Supervision – A.R., D.B.A., C.Ş.T., A.T., A.V., S.T.; Data Collection and/or Processing – A.R., D.B.A., S.T.; Analysis and/or Interpretation – A.R., D.B.A., A.V., S.T.; Literature Search – A.R., D.B.A., C.Ş.T., A.T., A.V., S.T.; Writing Manuscript – A.R., D.B.A., C.Ş.T., A.T., A.V., S.T.; Critical Review – A.R., D.B.A., C.Ş.T., A.T., A.V., S.T.

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