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Original Article

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Effects of a Change in the Definition of Chronic Kidney Disease on Geriatric Assessment Parameters

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ABSTRACT

Objectives: Geriatric syndromes are common in elderly subjects with chronic kidney disease. An age-adapted definition of chronic kidney disease has recently been proposed. This study aimed to investigate the effects of this change in the definition of chronic kidney disease (from an estimated glomerular filtration rate of <60 to <45 mL/min/1.73 m^2) on geriatric assessments.

Methods: Records of an elderly outpatient population were retrospectively reviewed. Subjects underwent comprehensive geriatric assessment including the Basic and Instrumental Activities of Daily Living, Mini-Mental State Examination, Geriatric Depression Score, Tinetti Mobility test, the Timed Up and Go test, the Mini Nutritional Assessment, the handgrip test, and the Insomnia Severity Index. Logistic regression analysis was performed in order to determine the odds ratio of each chronic kidney disease definition on geriatric syndromes.

Results: Of the 1222 patients, 832 (68.1%) were women and the median age was 73 (interquartile range, 67-80) years. Patients with an estimated glomerular filtration rate of <45 and <60 mL/min/1.73 m^2 comprised 8.3% (n = 101) and 21.6% (n = 264) of the cohort, respectively. Both estimated glomerular filtration rates of <45 and <60 mL/min/1.73 m^2 were significantly associated with more unfavorable geriatric assessment scores in univariate analysis. After adjustments, associations of an estimated glomerular filtration rate <60 mL/min/1.73 m^2 with the Timed Up and Go test and polypharmacy remained significant; however, none of the geriatric assessment measures remained significantly associated with an estimated glomerular filtration rate of <45 mL/min/1.73 m^2.

Conclusion: Chronic kidney disease was more significantly associated with impairments in geriatric assessment parameters when the cut-off of estimated glomerular filtration rate for the definition of chronic kidney disease was kept as <60 mL/min/1.73 m^2 in comparison to modification of <45 mL/min/1.73 m^2.

Keywords: Aged, geriatric assessment, kidney impairment

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INTRODUCTION

Aging is associated with significant changes in both structure and functions of the kidney, irrespective of any comorbidities.[1] Despite the decline in nephron number and the total measured glomerular filtration rate (GFR), single-nephron GFR remains relatively constant with healthy aging. In the absence of albuminuria, age-related reduction in GFR has been shown to be associated with a very modest to no increase in age-standardized risk of mortality or progression to end-stage kidney disease.[1] Thus, it was proposed that an age-related decrease in GFR may not signify chronic kidney disease (CKD) in some people.[2] Some literature commends to keep the current definition and states that the evaluation and management of CKD, not the definition, should be age-adapted.[3] From the GFR standpoint, an estimated GFR of <60 mL/min/1.73 m^2 for >3 months is considered as CKD,[4] but this definition is controversial.[4] With the

observation that mortality is increased at GFR <75 mL/min/1.73 m^2 among younger subjects and at levels <45 mL/min/1.73 m^2 in elderly, Delaneye et al[5] recently recommended that the definition of CKD should include age-specific thresholds for GFR. Indeed, a cut-off GFR of <60 mL/min/1.73 m^2 based on only one measurement may cause a high level of false-positive diagnoses of CKD, which would cause unnecessary utilization of healthcare resources.[6] Early CKD based on this definition comprises a significant portion of elderly subjects.[7]

Although geriatric syndromes are common among elderly patients with CKD, geriatric assessment measures are rarely performed in nephrology practice. Some of these measures may have a significant impact on overall patient survival.[8-10] Although several studies have reported results of particular geriatric assessment methods on patients with CKD, only a few have studied all of these tests comprehensively. The present study aimed to investigate the impact of change in the eGFR cut-off for the definition of CKD on associations with geriatric assessment parameters among elderly subjects in outpatient settings.

METHODS

Elderly subjects who were ≥65 years of age and attended one geriatric outpatient clinic between 2016 July and 2017 August were included. Among the 1812 subjects evaluated, exclusion criteria were as follows: dementia, Parkinson's disease, acute events that may alter the results of geriatric assessment tools (including respiratory failure, acute liver failure, sepsis, and malignancy conditions), lack of serum creatinine measurement, and end-stage CKD. Finally, 1222 subjects were included. The flowchart of the study is shown in Figure 1. Our study was approved by the Institutional Review Board of Bezmialem Vakıf University School of Medicine on June 26, 2019 and informed consent was taken from patients and their relatives/caregivers in order to use medical data.

All measurements were carried out during the outpatient visit and comprehensive geriatric assessments (CGA) were performed at the same time. The GFR was estimated from a single measurement of serum creatinine using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula.[11] Chronic kidney disease was defined and graded as an eGFR of <60 mL/min/1.73 m^2 according to guidelines.[4] Based on recent observations,[5] we used a second definition for this study that is an eGFR of <45 mL/min/1.73 m^2.

Participants underwent a CGA. The cores of this assessment and definitions are as follows:

Timed Up and Go Test: Functional mobility was measured using the Timed Up and Go (TUG) test. The patient was timed during rising from an armchair, walking at a comfortable and safe pace in a line on the floor 3 m away, then turning and walking back to the chair, and sitting down. A score of ≥13.5 seconds was considered abnormal which refers to high risk of falling.[12,13]

Tinetti Performance Oriented Mobility Assessment (POMA): The scale evaluates 7 components of gait (initiation of gait, step length, step symmetry, step continuity, path, trunk, and walking stance; a maximum of 12 points) and 9 components of balance (sitting balance, arises, attempts to arise, immediate standing balance, standing balance, nudged, eyes closed, turning 360°, and sitting down; a maximum of 16 points). Each component was counted as abnormal = 0 or normal = 1; in some cases, adaptive = 1 and normal = 2. The sum of total gait and balance scores equals a maximum of 28 points. A total score of <19 was counted as high risk and refers to high risk of falling.[14,15]

Recurrent falls: Recurrent falls were defined as existing if the patient had at least 2 falls within the previous year excluding tripping on a rug and slipping on a wet floor.[16]

The Handgrip test: Grip strength was measured using a Lafayette Hydraulic grip dynamometer (Ind, USA). A score of <27 for men and <16 for women was accepted as probable sarcopenia according to the Revised European Working Group's criteria for Sarcopenia Studies in Older People.[17]

The Barthel Index for basic activities of daily living (BADL) scale evaluates the ability to provide self-care, use toilet, get dressed, eat, urinary and fecal continence, use the stairs, move from bed to chair, and mobility and includes totally 10 questions.[18,19] Functional dependence based on BADL is classified as follows:

- 0-20 points, completely dependent;
- 21-61 points, severely dependent;
- 62-90 points, moderately dependent;
- 91-99 points, mildly dependent;
- 100 points, independent.

The Lawton–Brody instrumental activities of daily living (IADL) index considers telephone usage, preparing meals, shopping,

MAIN POINTS

- A considerable number of elderly subjects are categorized as chronic kidney disease (CKD) when CKD is defined according to the estimated glomerular filtration rate (eGFR) as an eGFR of <60 mL/min/1.73 m^2. Some authors propose an age-adapted definition to avoid misdiagnosis and inappropriate care.
- In this study, CKD was more significantly associated with impairments in geriatric assessment parameters when the cut-off of eGFR for the definition of CKD was kept as <60 mL/min/1.73 m^2 in comparison to a modification of <45 mL/min/1.73 m^2.
- Measures of geriatric syndromes appear to denote abnormalities with a decline in estimated glomerular filtration rate to <60 mL/min/1.73 m^2.

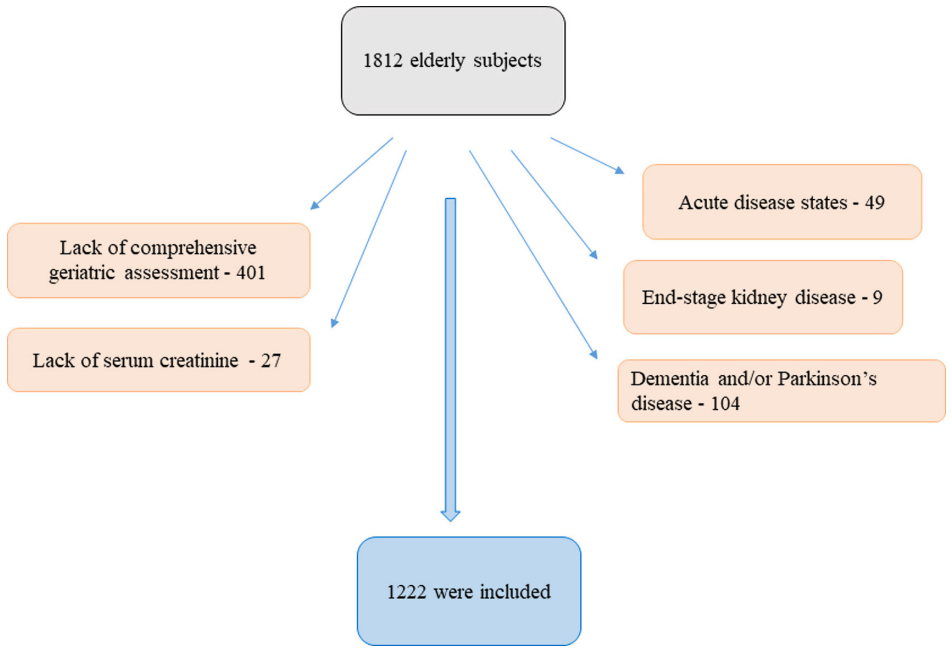

Figure 1. Flowchart of the study.

doing daily house works, laundry, transportation, taking pills, and money management and includes 8 questions.[20,21] According to IADL, patients are grouped as follows:

- 0-8 points, dependent;
- 9-16 points, semi-dependent;
- 17-24 points, independent.

The diagnosis of mild cognitive impairment was based on the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria.[22]

Mini Nutritional Assessment: A score of ≤23 was counted as abnormal and comprises subjects with increased risk of malnutrition and subjects with malnutrition.[23,24]

Frailty: Frailty status was determined according to 5 dimensions of frailty phenotype as follows: shrinking, exhaustion, low levels of physical activity, weakness, and slowness. People with 0 criteria were counted as robust, 1-2 as prefrail, and ≥3 as frail.[25]

Geriatric Depression Scale: Geriatric Depression-15 Scale (GDS-15), which is the short version of GDS-30, was used. A score of ≥5 was considered as depression in the Turkish population.[26]

Insomnia Severity Index: This index consists of 7 questionnaire items that capture self-reported symptoms and daytime consequences of insomnia. Insomnia Severity Index (ISI) scores range from 0 to 28, with higher scores indicating more severe insomnia. ISI scores of ≥8 indicated the presence of insomnia.[27-29]

Polypharmacy: An exposure to ≥5 drugs was considered polypharmacy.[30]

Orthostatic hypotension: Orthostatic hypotension was defined as a decrease in blood pressure of ≥20 mm Hg systolic and/or ≥10 mm Hg diastolic within 3 minutes following standing compared with the sitting or supine position.[31]

The Charlson Comorbidities Index was applied in order to evaluate the comorbidity burden.[32]

Demographic characteristics (age, sex, years of education) comorbidities and laboratory measurements that belong to the same visit of comprehensive geriatric assessments were also recorded.

Statistical Analysis

Quantitative variables are expressed as median with the interquartile range (IQR, 25%-75%). Qualitative variables are expressed as proportions. Groups were compared for means using Mann–Whitney *U* test. For comparisons between proportions, chi-squared tests or Fisher's exact test were used, as appropriate. For each geriatric test, outcomes were dichotomized according to validated thresholds. Logistic regression analysis was performed in order to assess the association of each CKD definition with geriatric impairments. In addition to age and sex, variables that had a significant association with CKD in the univariate analysis were included in the multivariate regression model, and a stepwise method was applied. Results were expressed as odds ratios (OR) and 95% CIs for logistic regression. Statistical analysis was performed using

Statistical Package for the Social Sciences 22.0 version (IBM Corp., Armonk, NY, USA). A *P* value of .05 was considered to be statistically significant.

RESULTS

General Characteristics

Of the 1222 patients, 832 (68.1%) were women and the median age was 73 (IQR, 67-80) years. Median serum creatinine and eGFR of the total sample were 0.77 mg/dL (IQR, 0.64-0.97) and 82 mL/min/1.73 m^2 (IQR, 64-93), respectively. Patients with an eGFR of <45 and <60 mL/min/1.73 m^2 comprised 8.3% (101 patients) and 21.6% (264 patients) of the total sample, respectively.

In the comparisons between patients with an eGFR of ≥60 mL/min/1.73 m^2 versus <60 mL/min/1.73 m^2 (Table 1), the latter group were found to be older (median age, 78 vs. 72; *P* < .001) and were more likely to have hypertension (76.9% vs. 65.5%), ischemic heart disease (18.7% vs. 12.0%, *P* = .005), cerebrovascular disease (10.0% vs. 5.3%, *P* = .006), and a higher Charlson comorbidity index (median, 1 vs. 0; *P* < .001). Among laboratory measurements, patients with an eGFR of <60 mL/min/1.73 m^2 had a lower hemoglobin (median, 13 vs. 14 g/dL; *P* < .001), lower folic acid (median, 7.2 vs. 8.8, ng/mL; *P* < .001), and higher vitamin B12 (median, 269 pg/mL vs. 217; *P* < .001). In the comparisons between eGFR ≥ 45 versus eGFR < 45 mL/min/1.73 m^2 groups, patients in the latter group were found to be older (median, 80 vs. 73; *P* < .001) and were more likely to have hypertension (77.6% vs. 67.0%, *P* = .032) and cerebrovascular disease (11.2% vs. 5.8%, *P* = .034). Patients with an eGFR of <45 mL/min/1.73 m^2 had a lower diastolic blood pressure (median, 74 vs. 80 mmHg; *P* = .026), lower hemoglobin (median, 10 vs. 13 g/dL; *P* < .001), lower serum folic acid (median, 7.1 vs. 8.7 ng/mL; *P* < .001), and higher serum vitamin B12 levels (median, 296 vs. 225, pg/mL; *P* = .007).

Table 1. Demographic and Clinical Characteristics of Subjects According to 2 Different Cut-Off Values of Glomerular Filtration Rate

	Total Sample (N = 1222)	GFR ≥ 60 (N = 958)	GFR < 60 (N = 264)	*P*	GFR ≥ 45 (N = 1121)	GFR < 45 (N = 101)	*P*
Age, years	73 (67-80)	72 (66-78)	78 (73-84)	**<.001**	73 (67-79)	80 (75-86)	**<.001**
Female sex, n, %	67.9	68.9	64.4	.192	67.5	72.3	.345
Education, years	3 (0-5)	3 (0-5)	3 (0-5)	.261	3 (0-5)	0 (0-5)	.284
Hypertension, n/N, %	67.9	65.5	76.9	**.001**	67.0	77.6	**.032**
Diabetes, n/N, %	36.1	34.8	40.6	.089	36.1	35.7	.941
Heart failure, n/N, %	6.0	5.6	8.4	.102	6.2	6.1	.987
Ischemic heart disease, n/N, %	13.4	12.0	18.7	**.005**	13.2	16.3	.378
COPD, n/N, %	13.3	14.3	13.0	.581	14.2	12.5	.650
Cerebrovascular disease, n/N, %	6.3	5.3	10.0	**.006**	5.8	11.2	**.034**
Charlson Comorbidity Index	1 (0-1)	0 (0-1)	1 (0-2)	**<.001**	1 (0-1)	1 (0-2)	.186
Systolic blood pressure, mm Hg	140 (120-160)	140 (120-160)	140 (120-160)	.767	140 (120-160)	140 (120-160)	.266
Diastolic blood pressure, mm Hg	80 (70-90)	80 (70-90)	80 (70-90)	.224	80 (70-90)	74 (70-80)	**.026**
Body mass index, kg/m^2	31.2 (27.4-35.4)	31.3 (27.6-35.4)	30.5 (26.4-34.8)	.119	31.2 (27.5-35.4)	29.7 (25.3-34.3)	.067
Serum creatinine, mg/dL	0.77 (0.64-0.97)	0.71 (0.61-0.83)	1.19 (1.03-1.45)	**<.001**	0.74 (0.62-0.91)	1.51 (1.30-1.85	**<.001**
eGFR, mL/min/1.73/m^2	83 (64-93)	87 (78-94)	49 (40-56)	**<.001**	85 (70-93)	35 (30-41)	**<.001**
Hemoglobin, g/dL	13.8 (12.7-14.9)	14 (13-15)	13 (12-14)	**<.001**	13.9 (12.8-14.9)	12.7 (11.4-13.9)	**<.001**
Vitamin D, ng/mL	12 (9-22)	13 (9-22)	10 (9-22)	.156	13 (9-22)	10 (9-21)	.448
HbA1-c, %	6.2 (5.7-7.3)	6.2 (5.7-7.2)	6.3 (5.8-7.5)	.279	6.2 (5.7-7.5)	6.1 (5.7-7.0)	.278
Folic acid, ng/mL	8.6 (6.4-11.1)	8.8 (6.6-11.3)	7.2 (5.5-9.7)	**<.001**	8.7 (6.5-11.2)	7.1 (5.4-9.4)	**<.001**
Vitamin B12, pg/mL	229 (164-338)	217 (161-320)	269 (181-400)	**<.001**	225 (163-327)	296 (169-421)	**.007**

Continuous variables are presented as median with the interquartile range (25%-75%).
COPD, chronic obstructive lung disease; eGFR, estimated glomerular filtration rate.
A *P* value of <0.05 is considered as statistically significant, and is shown in bold.

The majority of comprehensive geriatric assessment measures were more likely to suggest impairment in the group with an eGFR of <60 mL/min/1.73 m^2 versus ≥60 mL/min/1.73 m^2 and in the group with an eGFR <45 mL/min/1.73 m^2 versus ≥45 mL/min/1.73 m^2 (Table 2). An eGFR of <60 (vs. ≥60) mL/min/1.73 m^2 and an eGFR of <45 (vs. ≥45) mL/min/1.73 m^2 were significantly associated with numerous geriatric syndromes in univariate analysis (Table 3). When adjusted for age and sex, an eGFR of <60 mL/min/1.73 m^2 was still significantly associated with mild cognitive impairment (OR, 1.54; 95% CI, 1.09-2.16; *P* = .014), abnormal TUG test score (OR, 1.86; 95% CI, 1.34-2.58; *P* < .001), and polypharmacy (OR, 2.06; 95% CI, 1.53-2.78; *P* < .001). After adjustments for age, sex, hypertension, ischemic heart disease, cerebrovascular disease, Charlson comorbidity index, serum vitamin B12, serum folic acid, and hemoglobin, the association of an eGFR <60 mL/min/1.73 m^2 with TUG test (OR, 1.47; 95% CI, 1.02-2.13; *P* = .040) and polypharmacy (OR, 1.43; 95% CI, 1.00-2.05; *P* = .048) remained significant. For an eGFR of <45 mL/min/1.73 m^2, polypharmacy (OR, 1.70; 95% CI, 1.10-2.64; *P* = .018) and recurrent falls (OR, 1.61; 95% CI, 1.04-2.50; *P* = .032) were significant associations when adjusted for age and sex. None of the geriatric assessment

Table 2. Association of Kidney Impairment Defined with Different Glomerular Filtration Rate Cut-Off Values with Comprehensive Geriatric Aassessment Tools

	Total Sample	GFR ≥ 60 (n = 958)	GFR < 60 (n = 264)	*P*	GFR ≥ 45 (n = 1121)	GFR < 45 (n = 101)	*P*
MNA total	25 (22-27)	25 (23-27)	24 (21-27)	**<.001**	25 (22-27)	24 (19-27)	**.003**
No malnutrition, % Risk of malnutrition, % Malnutrition, %	65.7 27.7 6.6	68.2 26.5 5.3	56.6 31.9 11.5	**<.001**	66.% 27.7 5.9	56.5 28.2 15.3	**.003**
Insomnia Severity Index	12 (5-19)	11 (5-19)	15 (7-19)	.125	12 (5-19)	16 (7-19)	.731
Insomnia, %	62.8	60.9	71.8	.060	62.6	68.2	.595
Frail total	1 (0-3)	1 (0-3)	2 (0-5)	**<.001**	1 (0-3)	3 (1-4)	**<.001**
No frailty, % Prefrail, % Frail, %	31.9 38.2 29.9	34.5 39.0 26.5	19.4 34.5 46.0	**<.001**	32.8 38.6 28.6	17.0 31.9 51.1	**.003**
GDS	4 (1-8)	4 (1-8)	4 (1-9)	.075	4 (1-8)	4 (1-9)	.634
Depression, %	38.3	37.4	41.8	.253	38.0	41.3	.572
MMSE	25 (22-28)	26 (23-28)	24 (20-26)	**<.001**	26 (23-28)	23 (19-36)	**<.001**
IADL	19 (14-22)	20 (16-22)	16 (8-20)	**<.001**	19 (15-22)	14 (8-20)	**<.001**
BADL	92 (85-98)	95 (85-100)	89 (75-95)	**<.001**	93 (85-100)	85 (73-95)	**<.001**
Number of urination/night	2 (1-3)	2 (1-3)	2 (1-4)	.484	2 (1-3)	2 (1-4)	.326
Nocturia, %	67.8	67.3	69.7	.468	68.5	60.2	.093
Urinary incontinence, %	52.4	52.4	52.5	.962	52.5	51.0	.772
Handgrip	20 (16-26)	21 (17-27)	19 (14-23)	**<.001**	20 (16-26)	19 (13-24)	**.005**
Probable sarcopenia, %	34.2	25.5	46.9	**<.001**	33.6	41.7	.134
Tinetti Balance	12 (10-12)	12 (11-12)	12 (9-12)	.198	12 (11-12)	12 (8-14)	.804
Tinetti Gait	15 (12-16)	15 (13-16)	12 (10-15)	**<.001**	15 (12-16)	12 (9-14)	**<.001**
Tinetti Total	27 (23-28)	27 (25-28)	25 (19-28)	**<.001**	27 (24-28)	25 (16-28)	**<.001**
TUG	12 (9-16)	11 (9-15)	14 (11-20)	**<.001**	12 (9-15)	15 (11-24)	**<.001**
Number of drugs	4 (2-6)	4 (2-6)	5 (3-8)	**<.001**	4 (2-6)	5 (3-8)	**<.001**
Polypharmacy, % Hyperpolypharmacy, %	33.4 3.3	29.5 2.5	48.0 6.6	**<.001** **.002**	32.2 3.0	46.8 7.4	**.004** **.032**
Orthostatic hypotension, %	35.3	34.2	39.7	.132	35.5	32.9	.636
Recurrent falls, %	28.5	26.8	34.6	**.014**	27.2	42.9	**.001**

Continuous variables are presented as median with the interquartile range (25%-75%).
BADL, Basic Activity of Daily Living (Bartel); GDS, Geriatric Depression Scale; IADL, Instrumental Activity of Daily Living (Lawton); MMSE, Mini-Mental State Examination; MNA, Mini Nutritional Assessment; TUG, Ttimed Up and Go.
A *P* value of <0.05 is considered as statistically significant, and is shown in bold.

Table 3. Unadjusted and Adjusted Logistic Regression Models for the Association with Different Stages of Kidney Disease

	GFR < 60 mL/min/1.73 m²; Unadjusted			GFR < 60 mL/min/1.73 m²; Adjusted[a]			GFR < 60 mL/min/1.73 m²; Adjusted[b]			GFR < 45 mL/min/1.73 m²; Unadjusted			GFR < 45 mL/min/1.73 m²; Adjusted[a]			GFR < 45 mL/min/1.73 m²; Adjusted[c]		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Malnutrition	**1.63**	**1.21-2.22**	**.001**	1.26	0.91-1.74	.162	1.01	0.69-1.47	.963	1.53	0.98-2.40	.064	0.99	0.61-1.59	.959	0.63	0.34-1.16	.137
Probable sarcopenia	**1.98**	**1.45-2.70**	**<.001**	1.39	0.99-1.96	.058	1.10	0.74-1.65	.634	1.42	0.90-2.23	.135	0.89	0.53-1.47	.645	0.69	0.37-1.29	.243
Insomnia	1.63	0.98-2.73	.062	1.59	0.93-2.70	.088	1.33	0.75-2.37	.333	1.28	0.51-3.21	.596	1.17	0.46-2.98	.748	0.94	0.33-2.71	.907
Frailty	**2.37**	**1.63-3.44**	**<.001**	1.33	0.87-2.04	.192	1.03	0.64-1.68	.897	**2.61**	**1.44-4.72**	**.002**	1.07	0.55-2.10	.836	0.61	0.27-1.37	.230
Depression	1.20	0.88-1.64	.253	1.17	0.84-1.62	.352	1.01	0.70-1.45	.973	1.15	0.71-1.85	.572	1.04	0.64-1.71	.869	0.89	0.50-1.59	.688
MCI	**2.12**	**1.54-2.91**	**<.001**	**1.54**	**1.09-2.16**	**.014**	1.33	0.90-1.95	.150	2.41	1.49-3.90	**<.001**	1.47	0.88-2.44	.138	1.22	0.67-2.20	.515
Tinetti total	**2.25**	**1.53-3.30**	**<.001**	1.33	0.87-2.03	.185	0.94	0.63-1.65	.937	2.96	1.79-4.91	**<.001**	1.53	0.87-2.66	.136	1.29	0.67-2.49	.452
TUG	**2.81**	**2.08-3.78**	**<.001**	**1.86**	**1.34-2.58**	**<.001**	**1.47**	**1.02-2.13**	**.040**	**2.35**	**1.53-3.62**	**<.001**	1.18	0.73-1.90	.494	0.73	0.41-1.31	.294
Polypharmacy	**2.20**	**1.65-2.93**	**<.001**	**2.06**	**1.53-2.78**	**<.001**	**1.43**	**1.00-2.05**	**.048**	**1.85**	**1.21-2.83**	**.004**	**1.70**	**1.10-2.64**	**.018**	1.06	0.61-1.83	.834
OH	1.27	0.93-1.73	.133	1.14	0.83-1.57	.430	1.14	0.80-1.62	.485	0.89	0.55-1.44	.636	0.76	0.47-1.25	.284	0.62	0.35-1.09	.096
Recurrent falls	**1.45**	**1.08-1.95**	**.015**	1.24	0.91-1.69	.172	1.03	0.73-1.46	.866	**2.01**	**1.32-3.06**	**.001**	**1.61**	**1.04-2.50**	**.032**	1.46	0.86-2.49	.165

[a]Adjusted for sex and age; [b]After adjustment for age, sex, hypertension, ischemic heart disease, cerebrovascular disease, Charlson comorbidity index, serum vitamin B12 levels, serum folic acid levels, and hemoglobin; [c]After adjustment for age, sex, vitamin B12, folic acid, and hemoglobin.
TUG, Ttimed Up and Go; MCI, mild cognitive impairment; OH, orthostatic hypotension.
A *P* value of <0.05 is considered as statistically significant, and is shown in bold.

measures remained significantly associated with an eGFR of <45 mL/min/1.73 m^2 after adjustments for age, sex, serum vitamin B12 levels, serum folic acid levels, and hemoglobin.

A comparison was made between early stage CKD (eGFR, 45-60 mL/min/1.73 m^2) and late stage CKD (eGFR, <45 mL/min/1.73 m^2). Patients with late stage CKD were significantly older (median age, 80 vs. 77 years; *P* = .001) and female (72.3% vs. 60.1%; *P* = .045). For geriatric syndromes, only history of recurrent falls was more common in subjects with late stage CKD (42.9% vs. 30.1%, *P* = .038).

DISCUSSION

This study showed that the selection of an eGFR of <45 (mL/min/1.73 m^2) for the diagnosis of CKD among elderly subjects does not substantially change the interpretation of comprehensive geriatric assessment scores when compared with the cut-off value of <60 mL/min/1.73 m^2. Our results support the study by König et al.[7] who found that an early CKD state (eGFR of 45-59 mL/min/1.73 m^2) is associated with a poor performance in relation to the TUG test even after adjustment for important covariates. This is not dissimilar to our results. Moreover, this study evaluated detailed clinical data including folic acid and vitamin B12 levels, insufficiency of which may cause numerous negative effects on geriatric assessment parameters. Some authors believe that the current definition of CKD based on eGFR may cause overdiagnosis and lead to unnecessary usage of sources.[2,5] They propose that a change in the definition to <45 mL/min/1.73 m^2 would be reasonable, given the expected decline in eGFR even in those who do not have kidney disease. Our study is the first to evaluate the effects of such a change. Determining the optimal cut-off level for GFR is essential and would have a huge impact worldwide. While we have not intended to shed light on such a hard question, we could confirm that some of the measures of comprehensive geriatric assessment start to turn abnormal when the eGFR cut-off is kept at 60 mL/min/1.73 m^2 but not when the eGFR cut-off is changed to 45 mL/min/1.73 m^2.

Approximately 20% of the present sample had CKD when the definition is accepted as an eGFR of <60 mL/min/1.73 m^2. This rate was around 16% in the Berlin Aging Study II when the GFR was estimated with the CKD-EPI formula.[33] This formula may overestimate GFR in the elderly.[33] Indeed, in the Berlin Aging Study II by Konig and colleagues, the prevalence of CKD increased from 16% to 25% using other formulas which are preferred for the estimation of GFR in older subjects.[33] The mean age in their study was 68.7 years and 51.2% of their patients were female. The present study used the CKD-EPI equation which has been validated and widely used.[11] It is worth noting that albuminuria status which was not available in this study should be taken into account while capturing CKD, since it has prognostic implications.[34]

Comorbid illnesses may have contributed to our results. The Charlson activity index was significantly higher among patients with an eGFR of <60 versus ≥ 60 mL/min/1.73 m^2, while the significance was lost when the cut-off was 45. For instance, the frequency of ischemic heart disease was significantly different between CKD and non-CKD groups with the current definition but not when the cut-off was 45. Cardiovascular disease is associated with a higher risk of numerous geriatric syndromes,[35,36] some of which are mobility limitation and polypharmacy, which were significantly different among CKD and non-CKD groups in our study.

Multiple geriatric syndromes have been studied in patients with CKD, some of which are cognitive dysfunction[37-44] and nutrition.[9,45-48] Except polypharmacy, which is not unexpected to be more commonly observed in subjects with CKD, only gait impairment was independently associated with CKD in this study. This association remained even after adjustments when the cut-off of eGFR for the definition of CKD was kept as <60 mL/min/1.73 m^2. The significance was attenuated to the null when the definition was made as an eGFR of <45 mL/min/1.73 m^2. However, patients with later stages of CKD (eGFR of <45 mL/min/1.73 m^2) were more likely to have a history of recurrent falls. The association of CKD with abnormal gait phenotypes, slow gait speed, and high risk of falls has been shown by many others,[49-58] and CKD currently represents a unique syndrome with particular gait phenotypes which is associated with increased risk of falls.[55]

Given the retrospective design, a cause and effect relationship can not be proven solely with these findings. The definition of CKD was based on estimation using one measurement of serum creatinine rather than direct measurement. Other biomarkers such as cystatin C may be more adequate in order to evaluate geriatric impairments, particularly cognitive dysfunction.[59] Urine albumin excretion results were not available, which could have provided a more detailed risk classification. The majority of subjects with CKD in our cohort had stage 3 CKD with only 2.4% having stage 4 CKD according to the current definitions. Patients with more severe kidney disease usually present to the nephrology clinics rather than geriatrics. Thus, we cannot rule out a possible selection bias. The effects of different definitions of CKD on comprehensive geriatric assessment measures should be studied in cohorts that includes more patients with stage 4 CKD. The validity and reliability of a few comprehensive geriatric assessment measures in the Turkish population were not available for all scales. While we detected patients with probable sarcopenia, data of those who had definite sarcopenia and/or severe sarcopenia were not available.

CONCLUSION

A change of definition of CKD for elderly subjects from <60 to <45 mL/min/1.73 m^2 does not apparently bring advantages in terms of the demonstration of associations with a state of CKD and geriatric impairments. It is not known how a change in the definition of CKD impacts patient lives and current routine, but based on our results, keeping the cut-off as <60 mL/min/1.73 m^2

seems plausible in order to evaluate the effects of CKD on geriatric syndromes. This paper is the first to evaluate the effects of different CKD definitions on the association of CKD with geriatric measures. Further studies are needed to confirm our findings.

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Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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REFERENCES

1. Hommos MS, Glassock RJ, Rule AD. Structural and functional changes in human kidneys with healthy aging. *J Am Soc Nephrol*. 2017;28(10):2838-2844. [CrossRef]
2. Glassock RJ, Delanaye P, Rule AD. Should the definition of CKD be changed to include age-adapted GFR criteria? YES. *Kidney Int*. 2020;97(1):34-37. [CrossRef]
3. Levey AS, Inker LA, Coresh J. "Should the definition of CKD be changed to include age-adapted GFR criteria?": Con: the evaluation and management of CKD, not the definition, should be age-adapted. *Kidney Int*. 2020;97(1):37-40. [CrossRef]
4. Levey AS, de Jong PE, Coresh J, et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. *Kidney Int*. 2011;80(1):17-28. [CrossRef]
5. Delanaye P, Jager KJ, Bökenkamp A, et al. CKD: A call for an age-adapted definition. *J Am Soc Nephrol*. 2019;30(10):1785-1805. [CrossRef]
6. Benghanem Gharbi M, Elseviers M, Zamd M, et al. Chronic kidney disease, hypertension, diabetes, and obesity in the adult population of Morocco: how to avoid "over"- and "under"-diagnosis of CKD. *Kidney Int*. 2016;89(6):1363-1371. [CrossRef]
7. König M, Gollasch M, Spira D, et al. Mild-to-moderate chronic kidney disease and geriatric outcomes: analysis of cross-sectional data from the Berlin aging Study II. *Gerontology*. 2018;64(2):118-126. [CrossRef]
8. Brown CJ, Flood KL. Mobility limitation in the older patient: a clinical review. *JAMA*. 2013;310(11):1168-1177. [CrossRef]
9. Komatsu M, Okazaki M, Tsuchiya K, Kawaguchi H, Nitta K. Geriatric nutritional risk index is a simple predictor of mortality in chronic hemodialysis patients. *Blood Purif*. 2015;39(4):281-287. [CrossRef]
10. Panichi V, Cupisti A, Rosati A, et al. Geriatric nutritional risk index is a strong predictor of mortality in hemodialysis patients: data from the Riscavid cohort. *J Nephrol*. 2014;27(2):193-201. [CrossRef]
11. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612. [CrossRef]
12. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc*. 1991;39(2):142-148. [CrossRef]
13. Dokuzlar O, Koc Okudur S, Soysal P, et al. Factors that increase risk of falling in older men according to four different clinical methods. *Exp Aging Res*. 2020;46(1):83-92. [CrossRef]
14. Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. *J Am Geriatr Soc*. 1986;34(2):119-126. [CrossRef]
15. Yücel SD, Şahin F, Doğu B, Şahin T, Kuran B, Gürsakal S. Reliability and validity of the Turkish version of the performance-oriented mobility assessment I. *Eur Rev Aging Phys Act*. 2012;9(2):149-159. [CrossRef]
16. Unutmaz GD, Soysal P, Tuven B, Isik AT. Costs of medication in older patients: before and after comprehensive geriatric assessment. *Clin Interv Aging*. 2018;13:607-613. [CrossRef]
17. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(4):601. [CrossRef]
18. Küçükdeveci AA, Yavuzer G, Tennant A, Süldür N, Sonel B, Arasil T. Adaptation of the modified Barthel index for use in physical medicine and rehabilitation in Turkey. *Scand J Rehabil Med*. 2000;32(2):87-92. [CrossRef]
19. Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. *Md State Med J*. 1965;14:61-65.
20. Yardımcı E. *İstanbul'da Yaşayan Yaşlı Öğretmenlerin Sağlık Sonuçlarının Günlük Yaşam Aktiviteleri ve Aletli Günlük Yaşam Aktiviteleri ile Ilişkisi* [Tıpta Uzmanlık Tezi]. İstanbul: İstanbul Üniversitesi; 1995.
21. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9(3):179-186. [CrossRef]
22. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA:. American Psychiatric Association. 2013.
23. Sarikaya D, Halil M, Kuyumcu ME, et al. Mini nutritional assessment test long and short form are valid screening tools in Turkish older adults. *Arch Gerontol Geriatr*. 2015;61(1):56-60. [CrossRef]
24. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition*. 1999;15(2):116-122. [CrossRef]
25. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56(3):M146-M156. [CrossRef]
26. Durmaz B, Soysal P, Ellidokuz H, Isik AT. Validity and reliability of geriatric depression scale-15 (short form) in Turkish older adults. *North Clin Istanb*. 2018;5(3):216-220. [CrossRef]
27. Ozdemir PG, Boysan M, Selvi Y, Yildirim A, Yilmaz E. Psychometric properties of the Turkish version of the Sleep Hygiene Index in clinical and non-clinical samples. *Compr Psychiatry*. 2015;59:135-140. [CrossRef]
28. Morin CM, Belleville G, Bélanger L, Ivers H. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*. 2011;34(5):601-608. [CrossRef]

29. Dutoglu E, Soysal P, Smith L, et al. Nocturia and its clinical implications in older women. *Arch Gerontol Geriatr*. 2019;85:103917. [CrossRef]
30. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr*. 2017;17(1):230. [CrossRef]
31. Lanier JB, Mote MB, Clay EC. Evaluation and management of orthostatic hypotension. *Am Fam Phys*. 2011;84(5):527-536.
32. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383. [CrossRef]
33. König M, Gollasch M, Demuth I, Steinhagen-Thiessen E. Prevalence of impaired kidney function in the German elderly: results from the Berlin aging Study II (BASE-II). *Gerontology*. 2017;63(3):201-209. [CrossRef]
34. Chen TK, Sperati CJ, Thavarajah S, Grams ME. Reducing kidney function decline in patients With CKD: core curriculum 2021. *Am J Kidney Dis*. 2021;77(6):969-983. [CrossRef]
35. Flood KL, Rohlfing A, Le CV, Carr DB, Rich MW. Geriatric syndromes in elderly patients admitted to an inpatient cardiology ward. *J Hosp Med*. 2007;2(6):394-400. [CrossRef]
36. Welmer AK, Angleman S, Rydwik E, Fratiglioni L, Qiu C. Association of cardiovascular burden with mobility limitation among elderly people: a population-based study. *PLoS ONE*. 2013;8(5):e65815. [CrossRef]
37. Berger I, Wu S, Masson P, et al. Cognition in chronic kidney disease: a systematic review and meta-analysis. *BMC Med*. 2016;14(1):206. [CrossRef]
38. Brodski J, Rossell SL, Castle DJ, Tan EJ. A systematic review of cognitive impairments associated with kidney failure in adults before natural age-related changes. *J Int Neuropsychol Soc*. 2019;25(1):101-114. [CrossRef]
39. Kurella M, Chertow GM, Luan J, Yaffe K. Cognitive impairment in chronic kidney disease. *J Am Geriatr Soc*. 2004;52(11):1863-1869. [CrossRef]
40. Kurella Tamura M, Wadley V, Yaffe K, et al. Kidney function and cognitive impairment in US adults: the reasons for geographic and racial differences in stroke (REGARDS) study. *Am J Kidney Dis*. 2008;52(2):227-234. [CrossRef]
41. Madan P, Kalra OP, Agarwal S, Tandon OP. Cognitive impairment in chronic kidney disease. *Nephrol Dial Transplant*. 2007;22(2):440-444. [CrossRef]
42. McQuillan R, Jassal SV. Neuropsychiatric complications of chronic kidney disease. *Nat Rev Nephrol*. 2010;6(8):471-479. [CrossRef]
43. O'Lone E, Connors M, Masson P, et al. Cognition in people with end-stage kidney disease treated with hemodialysis: a systematic review and meta-analysis. *Am J Kidney Dis*. 2016;67(6):925-935. [CrossRef]
44. Yaffe K, Ackerson L, Kurella Tamura M, et al. Chronic kidney disease and cognitive function in older adults: findings from the chronic renal insufficiency cohort cognitive study. *J Am Geriatr Soc*. 2010;58(2):338-345. [CrossRef]
45. Hwang W, Cho MS, Oh JE, et al. Comparison of creatinine index and geriatric nutritional risk index for nutritional evaluation of patients with hemodialysis. *Hemodial Int*. 2018;22(4):507-514. [CrossRef]
46. Kuo IC, Huang JC, Wu PY, Chen SC, Chang JM, Chen HC. A low geriatric nutrition risk index is associated with progression to dialysis in patients with chronic kidney disease. *Nutrients*. 2017;9(11). [CrossRef]
47. Lin TY, Hung SC. Geriatric nutritional risk index is associated with unique health conditions and clinical outcomes in chronic kidney disease patients. *Nutrients*. 2019;11(11). [CrossRef]
48. Xiong J, Wang M, Zhang Y, et al. Association of geriatric nutritional risk index with mortality in hemodialysis patients: a meta-analysis of cohort studies. *Kidney Blood Press Res*. 2018;43(6):1878-1889. [CrossRef]
49. Ho JQ, Verghese J, Abramowitz MK. Walking while talking in older adults with chronic kidney disease. *Clin J Am Soc Nephrol*. 2020;15(5):665-672. [CrossRef]
50. Kutner NG, Zhang R, Huang Y, Painter P. Gait speed and mortality, hospitalization, and functional status change among hemodialysis patients: a US renal data system special study. *Am J Kidney Dis*. 2015;66(2):297-304. [CrossRef]
51. Kutner NG, Zhang R, Huang Y, Wasse H. Gait speed and hospitalization among ambulatory hemodialysis patients: USRDS special study data. *World J Nephrol*. 2014;3(3):101-106. [CrossRef]
52. Kutner NG, Zhang R, Huang Y, Wasse H. Falls among hemodialysis patients: potential opportunities for prevention? *Clin Kidney J*. 2014;7(3):257-263. [CrossRef]
53. Roshanravan B. Gait speed in patients with kidney failure treated with long-term dialysis. *Am J Kidney Dis*. 2015;66(2):190-192. [CrossRef]
54. Roshanravan B, Robinson-Cohen C, Patel KV, et al. Association between physical performance and all-cause mortality in CKD. *J Am Soc Nephrol*. 2013;24(5):822-830. [CrossRef]
55. Tran J, Ayers E, Verghese J, Abramowitz MK. Gait abnormalities and the risk of falls in CKD. *Clin J Am Soc Nephrol*. 2019;14(7):983-993. [CrossRef]
56. Viscogliosi G, De Nicola L, Vanuzzo D, et al. Mild to moderate chronic kidney disease and functional disability in community-dwelling older adults. The cardiovascular risk profile in Renal patients of the Italian Health Examination Survey (CARHES) study. *Arch Gerontol Geriatr*. 2019;80:46-52. [CrossRef]
57. Wickstrom JF, Sayles HR, Graeff-Armas LA, Yentes JM. The likelihood of self-reporting balance problems in those with advanced chronic kidney disease, slow gait speed, or low vitamin D. *J Ren Nutr*. 2019;29(6):490-497. [CrossRef]
58. Zemp DD, Giannini O, Quadri P, de Bruin ED. Gait characteristics of CKD patients: a systematic review. *BMC Nephrol*. 2019;20(1):83. [CrossRef]
59. Yaffe K, Kurella-Tamura M, Ackerson L, et al. Higher levels of cystatin C are associated with worse cognitive function in older adults with chronic kidney disease: the chronic renal insufficiency cohort cognitive study. *J Am Geriatr Soc*. 2014;62(9):1623-1629. [CrossRef]