BMC Nephrology

RESEARCH

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The prevalence of frailty according to kidney function and its association with cognitive impairment, nutritional status, and clinical outcome

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Abstract

Background Frailty is a state of vulnerability to poor homeostatic resolution of after a stressful event. The prevalence of frailty in patients with chronic kidney disease (CKD) is more common than in the general population. Frailty is associated with a poor clinical prognosis, malnutrition, and cognitive impairment; however, studies on these factors in patients with CKD are lacking. Therefore, we aimed to evaluate the relationship between CKD and frailty, nutritional status, and cognitive impairment and their influence on clinical outcomes.

Methods We prospectively enrolled participants from June 2019 to December 2020 and divided them into three CKD groups according to kidney function (CKD G1-2, CKD G3-4, and CKD G5D). Clinical outcomes were defined as the composite outcomes of all-cause death, hospitalization, and cardiovascular outcomes, including nonfatal myocardial infarction, revascularization, or stroke. To calculate the relative risk of frailty, cognitive impairment, nutritional status, and clinical outcome, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using logistic regression analysis.

Result A total of 83 patients were included, of whom 31.3% had frailty and 18.1% had cognitive impairment. In the CKD G5D group, the prevalence of frailty (56.7%, $n=17$) was significantly higher, and the nutritional quotient score was lower in the other groups. The Korean-Montreal Cognitive Assessment score was significantly lower in the CKD G5D group; however, cognitive impairment did not differ among the three groups. Frailty was significantly associated with cognitive impairment and CKD G5D group. Cognitive impairment was significantly associated with older age and higher BMI. Well-nourished status was significantly associated with BMI and CKD G5D group. Patients in the CKD G5D group were significantly more likely to have adverse clinical outcomes.

Conclusions The prevalence of frailty increased significantly as the CKD stage progressed. Particularly, CKD G5D group correlated with frailty and nutritional status, leading to poor clinical outcomes.

Keywords CKD, Frailty, Nutritional status, Cognitive impairment, Clinical outcomes

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Introduction

Frailty is a state of vulnerability to poor homeostatic resolution after a stressful event [1]. The prevalence of frailty varies with age, sex, income, and comorbidities [2–5], and has been reported to be 15% in elderly patients with chronic kidney disease (CKD), which is higher than the 6% in the elderly with normal kidney function [6]. In particular, in patients with end-stage kidney disease, the prevalence of frailty is high as 44.4%, even in those the age of 40 years, and increases sharply with age [7].

Frailty in CKD patients is a multifactorial condition. Uremic toxins and decreased cytokine clearance lead to increased levels of proinflammatory cytokines such as interleukin-6, and tumor necrosis factor alpha [8–10]. This contributes to the occurrence of sarcopenia and anorexia, and a reduced energy intake due to anorexia and dietary restrictions is associated with protein energy wasting (PEW) and frailty [11–13]. In addition, decreased production of and acquired resistance to anabolic hormones, and metabolic acidosis may lead to malnutrition and sarcopenia, which are ultimately associated with frailty [14].

Frailty in patients with CKD is associated with all-cause mortality and poor clinical outcomes such as hospitalization, impaired quality of life, and cognitive impairment [15–17]. However, there is a lack of research on the relationship between cognitive impairment and frailty in patients with CKD and on the mechanisms behind these associations. We aimed to evaluate the relationship between CKD and frailty, nutritional status, and cognitive impairment, and their influence on clinical outcomes. Therefore, using a prospective observational cohort study, we hypothesized that frailty, nutritional status, and cognitive impairment would differ depending on kidney function at baseline, and that these would be closely related to each other and ultimately be associated with a poor prognosis.

Materials and methods

Study population

This study prospectively enrolled adult (aged ≥ 18 years) outpatients visiting Gyeongsang National University Changwon Hospital from June 2019 to December 2020. Informed consent was obtained from each study participant. In patients who agreed to participate in the study, tests for diagnosing CKD, frailty tests, cognitive impairment tests, and interviews on nutritional status were conducted. In this process, patients who were unable or unwilling to provide written consent, had dementia ($n=4$), no available serum creatinine levels ($n=14$), no albuminuria ($n=5$) were excluded, and we followed up patients until January 2024 (Supplementary Fig. 1). This study was approved by the Institutional Review Board of Gyeongsang National University Hospital (IRB No. 2019–03-014–001).

Clinical parameters

Well-trained nurses investigated data on demographic and clinical characteristics, laboratory findings, and comorbidities through in-person interviews or by reviewing medical records at the time of enrollment. Body mass index (BMI) was calculated as weight (kg) ÷ [height (m)]^2. Systolic and diastolic blood pressure were measured using a mercury sphygmomanometer. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) study formula [1.86 × (plasma creatinine) − 1.154 × (age) − 0.203) × (0.74 if female) × (1.210 if black)]. We stratified kidney function by eGFR categories and divided patients into tertiles: CKD G1-2 (MDRD-GFR ≥ 90 mL/min/1.73m^2 and have albuminuria [albumin-to-creatinine ration ≥ 30 mg/g], MDRD-GFR 60-89 mL/min/1.73m^2), CKD G3-4 (MDRD-GFR 15-59 mL/min/1.73 m^2), and CKD G5 on dialysis (G5D) [18].

Frailty

Frailty was assessed by well-trained nurses using the Fried Frailty Index, which evaluates five components: unintentional weight loss, exhaustion, low physical activity, slow walking speed, and weak grip strength. Participants were classified as frail for weight loss if they reported losing more than 4.5 kg (10 pounds) unintentionally over the past year or if their calculated weight loss exceeded 5% of their body weight. Exhaustion was assessed using two items from the Center for Epidemiologic Studies Depression Scale, where participants were asked how often they felt that everything they did was an effort or that they could not get going, with a response of "3 or more days" per week considered indicative of frailty. Physical activity was assesses weekly energy expenditure from activities such as walking, gardening, and recreational sports. Participants were classified as frail if their weekly energy expenditure was less than 383 kcal for men or less than 270 kcal for women. Walking speed was evaluated over a 15-foot distance, with frailty thresholds stratified by gender and height: men were considered frail if they took 7 s or longer (height ≤ 173 cm) or 6 s or longer (height > 173 cm), while women were considered frail if they took 7 s or longer (height ≤ 159 cm) or 6 s or longer (height > 159 cm). Grip strength was measured using a hand dynamometer, with frailty cut-offs stratified by gender and BMI quartiles. For men, the cut-off values were ≤ 29 kg (BMI ≤ 24), ≤ 30 kg (BMI 24.1–28), and ≤ 32 kg (BMI > 28); for women, the cut-off

values were ≤ 17 kg (BMI ≤ 23), ≤ 17.3 kg (BMI 23.1–26), ≤ 18 kg (BMI 26.1–29), and ≤ 21 kg (BMI > 29) [19]. Participants meeting three or more of these five criteria were classified as frail, those meeting one or two criteria were classified as pre-frail, and those meeting none were classified as not frail [19, 20].

Cognitive impairment

The Montreal Cognitive Assessment (MoCA) was developed to determine mild cognitive impairment more accurately than the Mini-Mental State Examination (MMSE). The MoCA is a one-page 30-point test administered for 10 min. It consists of short-term memory(5 points; two learning trials of five nouns and delayed recall after approximately 5 min), visuospatial abilities (3 points: clock-drawing task; 1 point; three-dimensional cube copy), executive functions (1 point: trail making B task; 1 point: phonemic fluency task; 2 points: two-item verbal abstraction task), attention (1 point: sustained attention task; 3 points: serial subtraction task, 1 point each; digits forward and backward), language (3 points: three-item confrontation naming task; 2 points: repetition of two syntactically complex sentences), and orientation to time and place (6 points). Kang et al. developed the Korean-Montreal Cognitive Assessment (K-MoCA) and verified its reliability and validity in consideration of the cultural and linguistic characteristics of Koreans [21, 22]. In addition, they presented a cutoff value according to the level of education and age. In this study, the K-MoCA was used to determine cognitive impairment.

Nutritional status

Nutritional status was assessed using the Nutrition Quotient (NQ) for patients under the age of 65 years and NQ-elderly (NQ-E) for patients age of 65 years or older. The NQ and NQ-E are tools that comprehensively evaluate the nutritional status and meal quality of individuals or groups of adults according to their age (NQ for adults aged 19–64 years, NQ-E for adults over 65 years of age). The NQ and NQ-E were developed and validated by the Korean Society of Nutrition in 2018 based on data from the National Health and Nutrition Examination Survey [23, 24]. The NQ and NQ-E consisted of four categories (balance, diversity, moderation, and dietary behavior). The NQ consists of 21 items and nutritional status is evaluated as high, medium, and low, whereas the NQ-E consists of 19 items and nutritional status is evaluated as high, medium high, medium low, and low. We defined the patient's nutritional status as high, medium, or low by changing from medium high and medium low to medium in the NQ-E.

Clinical outcomes

The clinical outcomes were defined as the composite outcomes of all-cause death, hospitalization, and cardiovascular outcomes, including nonfatal myocardial infarction, revascularization, or stroke. Hospitalization and cardiovascular outcomes were identified based only on the occurrence of the first event; repeat hospitalizations and cardiovascular outcomes were not included. We also evaluated all-cause death, hospitalization, and cardiovascular outcomes separately.

Statistical analysis

Participants were divided into three groups based on their kidney function. The chi-square test and t-test were used to compare categorical and continuous clinical and laboratory parameters, respectively, among the three groups. Univariate and multivariate linear regression analyses were performed to investigate the association between clinical factors and frailty. The variables were selected using a forward conditional method. Statistical analyses were performed using the SPSS for Windows (ver. 25.0; IBM corp., Armonk, NY.). Statistical significance was defined as $P < 0.05$.

Results

Baseline characteristics according to kidney function

We prospectively enrolled 106 patients, and excluded 23 with underlying dementia, or no available serum creatinine levels, or no albuminuria (Supplementary Fig. 1). The mean age of the 83 patients included in this study was 62.8 years, and 59% were male. Regarding the patients' kidney function, 25 were assigned to the CKD G1-2 group, 28 to the CKD G3-4 group, and 30 to the CKD G5D group. The CKD G5D group had significantly lower serum hemoglobin, cholesterol, and albumin levels than the other groups. This group also had the highest percentage of patients with diabetes mellitus and hypertension. The proportion of patients with coronary artery disease and cerebrovascular disease was higher in the CKD G5D group than in the CKD G1-2 group but was highest in the CKD G3-4 group (Table 1). In the CKD G5D group, the median dialysis vintage was 19.6 months (0.0 – 172.4 months).

Frailty and kidney function

Frailty was observed in 26 patients (31.3%): 3 patients (12.0%) in the CKD G1-2 group, 6 patients (21.4%) in the CKD G3-4 group, and 17 patients (56.7%) in the CKD G5D group ($P = 0.003$) (Table 1, Fig. 1). CKD was significantly associated with frailty even after adjustment for covariates (Table 2). Among CKD groups, the CKD G5D group showed a significantly higher odds ratio (OR) of

Table 1 Baseline characteristics of the study population stratified by CKD group

Variables	Total (*N* = 83)	CKD G1-2 (*N* = 25)	CKD G3-4 (*N* = 28)	CKD G5D (*N* = 30)	*P*
Age (years)	62.8 ± 11.7	60.3 ± 12.3	64.9 ± 10.4	62.9 ± 12.3	0.369
Men, %	59.0	40.0	64.3	70.0	0.062
Education level, %					0.043
Less than elementary school	3.6	0.0	10.7	0.0	
Middle school	25.3	20.0	32.1	23.3	
High school	39.8	28.0	35.7	53.3	
College	31.3	52.0	21.4	23.3	
BMI (kg/m^2)	24.0 ± 4.1	24.4 ± 3.2	23.8 ± 4.2	23.7 ± 4.6	0.790
SBP (mmHg)	137.3 ± 20.3	131.6 ± 16.4	140.5 ± 21.3	139.0 ± 21.8	0.240
DBP (mmHg)	73.8 ± 15.1	74.9 ± 11.8	72.6 ± 13.1	73.8 ± 15.1	0.834
Frailty, %	31.3	12.0	21.4	56.7	0.003
Nutritional Quotient score	61.2 ± 8.9	62.0 ± 8.1	64.3 ± 9.6	57.8 ± 7.8	0.019
Nutritional status					0.079
High, %	38.6	52.0	46.4	20.0	
Medium, %	56.6	48.0	46.4	73.3	
Low, %	4.8	0.0	7.1	6.7	
Cognitive impairment, %	18.1	16.0	14.3	23.3	0.636
K-MoCA	23.6 ± 6.1	25.4 ± 5.0	23.1 ± 6.5	22.6 ± 6.4	0.199
Hemoglobin (g/dL)	11.8 ± 1.9	13.9 ± 1.3	11.6 ± 1.5	10.5 ± 1.0	< 0.001
Glucose (mg/dL)	135.6 ± 51.9	126.8 ± 64.8	129.9 ± 47.2	147.8 ± 44.1	0.268
Cholesterol (mg/dL)	157.5 ± 49.2	188.9 ± 48.3	156.8 ± 38.8	134.1 ± 46.5	< 0.001
Protein (g/dL)	6.9 ± 0.6	7.2 ± 0.5	6.8 ± 0.6	6.8 ± 0.6	0.001
Albumin (g/dL)	4.0 ± 0.5	4.4 ± 0.4	3.9 ± 0.4	3.8 ± 0.4	< 0.001
CRP (mg/L)	5.3 ± 15.5	0.9 ± 0.8	8.1 ± 16.3	6.4 ± 18.9	0.360
Hypertension, %	72.3	24.0	85.7	100.0	< 0.001
Diabetes, %	49.3	12.0	50.0	80.0	< 0.001
Coronary artery disease, %	18.1	0.0	28.6	23.3	0.008
Cerebrovascular disease, %	7.2	0.0	14.3	6.7	0.098
Malignancy, %	12.0	12.0	14.3	10.0	0.840

BMI body mass index, *CKD* chronic kidney disease, *CRP* C-reactive protein, *DBP* diastolic blood pressure, *K-MoCA* Korean-Montreal Cognitive Assessment, *SBP* systolic blood pressure, *5D* on dialysis

frailty compared to the CKD G1-2 group (OR, 9.67; 95% confidence interval [CI], 2.18 – 42.92; $P = 0.003$). In addition, frailty was significantly related to cognitive impairment (OR 4.79; 95% CI 1.28 – 17.93; $P = 0.020$), but other clinical factors, including nutritional status, were not significantly related (Table 2).

Cognitive impairment and kidney function

Cognitive impairment was observed in 15 patients (18.1%): 4 patients (16.0%) in the CKD G1-2 group, 4 patients (14.3%) in the CKD G3-4 group, and 7 patients (23.3%) in the CKD G5D group ($P = 0.636$) (Table 1, Fig. 1). The proportion of patients with cognitive impairment increased with decreased kidney function, but the difference was not statistically significant. The K-MoCA scores were also lower in the dialysis group than in the other groups, although this was not statistically significant (Table 1). Logistic regression analysis was used to evaluate factors associated with cognitive impairment. CKD was not significantly associated with cognitive impairment. Only age (OR 1.33, 95% CI 1.12 – 1.58, $P = 0.001$), and BMI (OR 1.39, 95% CI 1.08 – 1.79, $P = 0.010$) were related to cognitive impairment (Table 3).

Nutritional status and kidney function

The NQ score was lowest in the dialysis group, and the proportion of high nutritional status (well-nourished status) was also lower than in the other groups. (Table 1, Fig. 1, Supplementary Table 1).

Table 4 shows that CKD groups had a significant association with well-nourished status in the crude and fully adjusted models. The CKD G5D group had a significantly lower OR of a well-nourished status compared to the CKD G1-2 group (OR 0.14, 95% CI 0.04 – 0.53,

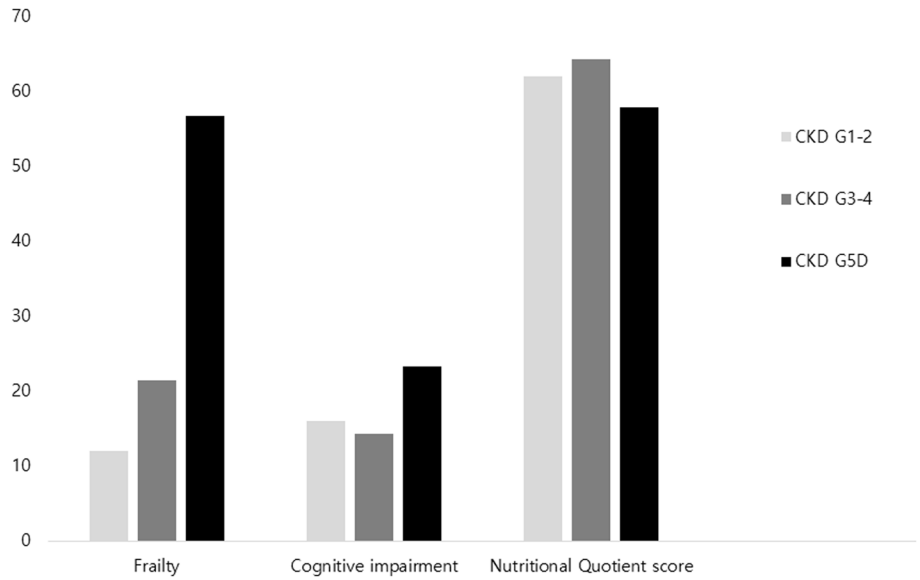

Fig. 1 The proportion of frailty and cognitive impairment and NQ score according to kidney function. Among CKD groups, the CKD 5D group had the highest proportion of frailty and cognitive impairment and the lowest Nutritional Quotient (NQ) score

Table 2 Odds ratios for frailty risk factors

	Univariate		Multivariate	
	OR (95% CI)	***P***	**OR (95% CI)**	***P***
Age (years)	1.04 (0.99 – 1.08)	0.105		
Sex, female (ref. male)	0.86 (0.33 – 2.22)	0.754		
Well-nourished status (ref. low to medium)	0.36 (0.13 – 1.02)	0.055		
Cognitive impairment (ref. no)	4.50 (1.40 – 14.50)	0.012	4.79 (1.28 – 17.93)	0.020
Hemoglobin (g/dL)	0.65 (0.48 – 0.88)	0.005		
Protein (g/dL)	0.34 (0.14 – 0.83)	0.017		
CKD group (ref. CKD G1-2)		0.002		0.003
CKD G3-4	2.00 (0.44 – 9.02)	0.367	2.04 (0.42 – 9.88)	0.421
CKD G5D	9.59 (2.35 – 39.12)	0.002	9.67 (2.18 – 42.92)	0.003

Adjusted for age, sex, nutritional status, cognitive impairment, serum hemoglobin, protein, CKD group

CI confidence interval, *CKD* chronic kidney disease, *OR* odds ratio, *5D* on dialysis

$P=0.004$). In univariate analysis, well-nourished status was significantly associated with cognitive impairment, serum albumin level, and CKD. However, only CKD groups and BMI (OR 0.86, 95% CI 0.74 – 0.98, $P=0.027$) were significantly associated with well-nourished status after adjusting for covariates.

Clinical outcomes

During the follow-up period of 28.7 ± 15.2 months, the composite clinical outcome was observed in 57.8% ($N=48$) of patients, of which all-cause death occurred in 6.0% ($N=5$), cardiovascular outcome occurred in 8.4% ($N=7$), and hospitalization occurred in 56.6% ($N=47$). Patients in the CKD G5D group were significantly more likely to achieve the composite clinical outcomes compared with the CKD G1-2 group (OR 5.48, 95% CI 1.68 – 17.87, $P=0.005$. In the univariate analysis, frailty, cognitive impairment, and nutritional status were not significantly associated with the clinical outcomes (Table 5). When evaluating the relationship between each component of clinical outcome and the CKD group, statistical significance was only observed for hospitalization and not for all-cause death or cardiovascular outcomes (Supplementary Table 2).

Table 3 Odds ratios for cognitive impairment

	Univariate		Multivariate	
	OR (95% CI)	***P***	**OR (95% CI)**	***P***
Age (years)	1.25 (1.11 – 1.41)	< 0.001	1.33 (1.12 – 1.58)	0.001
Sex, female (ref. male)	1.33 (0.43 – 4.09)	0.620		
BMI (kg/m^2)	1.19 (1.04 – 1.38)	0.015	1.39 (1.08 – 1.79)	0.010
Frailty (ref. no)	4.50 (1.40 – 14.50)	0.012		
Well-nourished status (ref. low to medium)	0.20 (0.04 – 0.93)	0.040		
CKD group (ref. CKD G1-2)		0.640		
CKD G3-4	0.88 (0.19 – 3.94)	0.862		
CKD G5D	1.60 (0.41 – 6.25)	0.501		
Cerebrovascular disease (ref. No)	5.42 (0.98 – 30.09)	0.053		

Adjusted for age, sex, BMI, frailty, nutritional status, CKD group, cerebrovascular disease

CI confidence interval, *CKD* chronic kidney disease, *OR* odds ratio, *5D* on dialysis

Table 4 Odds ratios for well-nourished status

	Univariate		Multivariate	
	OR (95% CI)	***P***	**OR (95% CI)**	***P***
Age (years)	0.98 (0.94 – 1.02)	0.296		
Sex, female (ref. male)	1.83 (0.75 – 4.51)	0.187		
BMI (kg/m^2)	0.90 (0.80 – 1.01)	0.074	0.86 (0.74 – 0.98)	0.027
Frailty (ref. no)	0.36 (0.13 – 1.02)	0.055		
Cognitive impairment (ref. no)	0.20 (0.04 – 0.93)	0.040		
Hemoglobin (g/dL)	1.12 (0.88 – 1.41)	0.364		
Albumin (g/dL)	3.15 (1.01 – 9.81)	0.047		
CKD group (ref. CKD G1-2)		0.038		0.012
CKD G3-4	0.80 (0.27 – 2.36)	0.686	0.57 (0.18 – 1.83)	0.349
CKD G5D	0.23 (0.07 – 0.76)	0.016	0.14 (0.04 – 0.53)	0.004

Adjusted for age, sex, BMI, frailty, cognitive impairment, serum hemoglobin, albumin, CKD group

CI confidence interval, *CKD* chronic kidney disease, *OR* odds ratio, *5D* on dialysis

Discussion

In this prospective outpatient cohort study, we explored the associations between kidney function and frailty, nutritional status, cognitive impairment, and clinical outcomes. We found that the prevalence of frailty increased in patients with CKD, especially in those receiving dialysis (CKD G5D group), and that impaired kidney function was significantly related to frailty, nutritional status, and clinical outcomes, but not with cognitive impairment.

Previous studies have shown that the prevalence of frailty, malnutrition, and cognitive impairment as well as clinical outcomes such as death, cardiovascular events, and hospitalization are higher in patients with CKD than in those without CKD [17, 25, 26]. Wilhelm-Leen et al. analyzed the association between frailty and CKD using data from the Third National Health and Nutrition Examination Survey. In this previous study, frailty was significantly associated with CKD, and both frailty and CKD were independently associated with mortality [20].

Kopple et al. examined protein-energy nutritional status according to kidney function in the Modification of Diet in Renal Disease Study, and showed that nutritional status declines as the kidney function decreases [27]. In another study, Tseng et al. assessed the relationship between frailty and nutritional status in patients with G3-5 CKD. They found that the PEW was significantly associated with frailty in CKD [28].

Coppolino et al. revealed that cognitive capacity decrease across CKD stages, and frailty is common in elderly patients with CKD [29]. In the general population, frailty and cognitive impairment have shown a close relationship in previous studies [30, 31]. However, research on the relationship between frailty and cognitive impairment in patients with CKD is lacking. In addition, there is still very little research on the relationship between

Table 5 Odds ratios for clinical outcomes

	Univariate		Multivariate	
	OR (95% CI)	***P***	**OR (95% CI)**	***P***
Age (years)	1.00 (0.96 – 1.04)	0.978		
Sex, female (ref. male)	1.17 (0.50 – 2.73)	0.723		
BMI (kg/m^2)	1.01 (0.91 – 1.12)	0.840		
Frailty (ref. no)	2.62 (0.95 – 7.20)	0.062		
Cognitive impairment (ref. no)	1.12 (0.36 – 3.49)	0.851		
Well-nourished status (ref. low to middle)	0.983 (0.42 – 2.32)	0.968		
Hemoglobin (g/dL)	0.70 (0.55 – 0.90)	0.006		
Albumin (g/dL)	0.35 (0.12 – 1.03)	0.056		
CKD group (ref. CKD G1-2)		0.002		0.019
CKD G3-4	3.11 (1.06 – 9.18)	0.040	2.22 (0.73 – 6.78)	0.063
CKD G5D	7.67 (2.42 – 24.25)	0.001	5.48 (1.68 – 17.87)	0.005
Hypertension (ref. no)	2.89 (1.07 – 7.79)	0.036		
Diabetes mellitus (ref. no)	2.37 (0.97 – 5.79)	0.059		

Adjusted for age, sex, BMI, frailty, serum hemoglobin, albumin, CKD group, hypertension, diabetes mellitus

CI confidence interval, *CKD* chronic kidney disease, *OR* odds ratio, *5D* on dialysis

frailty, nutritional status, and cognitive impairment according to kidney function, and its impact on clinical outcomes, including death.

Our study showed that at baseline, especially in the CKD G5D group, the proportion of frailty was higher and the NQ and K-MoCA scores were lower than those in the other groups, which is consistent with previous studies [12, 15, 17]. Unlike previous studies, the present study simultaneously evaluated frailty, nutritional status, cognitive impairment, and kidney function. However, these factors did not all exhibit a close relationship with each other; significant associations were seen between CKD and frailty, CKD and nutritional status, and cognitive impairment and frailty. Frailty, nutritional status, and cognitive impairment at the time of enrollment had no significant association with clinical outcomes; the only significant relationship with clinical outcomes was observed in the CKD G5D group compared with the CKD G1-2 group.

In summary of previous results, frailty, PEW, and cognitive impairment were significantly associated with CKD. However, studies comprehensively examining these factors are lacking. In this respect, our study has the advantage of comprehensively investigating the relationship between kidney function and other important factors in patients with CKD.

We suggest several explanations for the association between CKD and frailty, nutritional status, and clinical outcomes, but not cognitive impairment. First, CKD is not only a risk factor for frailty and malnutrition, but also shares pathophysiological mechanisms, such as oxidative stress, renin–angiotensin–aldosterone system activation, inflammation, and metabolic acidosis; therefore, they are closely related and influence each other, ultimately leading to poor clinical outcomes. Second, patients with CKD G5D showed the most significant correlation with clinical outcomes, and nutritional status. CKD G5D patients are educated on more strict dietary restrictions than non-dialysis CKD patients, and dietary intake is restricted to maintain appropriate serum phosphorus and potassium levels and to avoid excessive intradialytic weight gain. In addition, polypharmacy may also be associated with nutritional status and poor clinical outcomes. CKD G5D is a condition in which kidney function decline progresses further than non-dialytic CKD and progresses to kidney failure, and despite the development of hemodialysis technology and hemodialysis membranes, there is still a limit to the maintenance of biological homeostasis that the actual kidney is responsible for, so the risk of malnutrition, frailty, and death is considered to be higher in CKD G5D than in non-dialysis CKD. Third, cognitive impairment was observed at a higher proportion in CKD G5D patients than in other CKD groups, but there was no statistical significance. This may be because the duration of dialysis was short and relatively young patients were included, a correlation between kidney function and cognitive impairment may not have been present. The association with dementia in patients undergoing dialysis is usually explained by the hemodynamic instability during dialysis, decreased brain perfusion, and uremic toxicity. However, in our study, the median vintage of dialysis patients was 19.6 months, which means that maintenance dialysis duration was relatively short; this means that residual kidney function could be preserved,

decreasing the risk of uremia and intradialytic hypotension. Our study suggests that clinicians should pay attention to the frailty and nutritional status of patients with CKD, especially those requiring dialysis, regardless of age, as even relatively healthy patients receiving outpatient treatment warrant this attention. Additionally, since patients with CKD G5D have poor clinical outcomes compared to patients with non-dialysis CKD, clinicians should make efforts to delay CKD progression.

Our study had several limitations. First, due to the single-center design and to small number of observational cohort characteristics, the causality between kidney function and worsened frailty, nutritional status, and clinical outcomes cannot be determined and should be interpreted as a relationship. Second, our study enrolled relatively healthy patients who were eligible for outpatient treatment and did not include patients with severe frailty, malnourishment, or cognitive impairment. Third, our study investigated the relationship between cognitive impairment and kidney function at baseline and did not assess cognitive function at follow-up. Therefore, caution is needed when interpreting the relationship between kidney function and cognitive impairment, and additional research is needed in the future. Despite these limitations, the strength of our study was that we examined the relationship between kidney function and frailty, nutritional status, cognitive impairment, and clinical outcomes.

Conclusions

This study showed that CKD, especially CKD G5D, is significantly associated with frailty, nutritional status, and poor clinical outcomes. This suggests that we need to focus more on frailty, nutrition, and prevention of progression to kidney failure in patients with CKD.

Abbreviations

BMI	Body mass index
CKD	Chronic kidney disease
eGFR	Estimated glomerular filtration rate
K-MoCA	Korean-Montreal Cognitive Assessment
MDRD	Modification of Diet in Renal Disease
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
NQ	Nutritional Quotient
NQ-E	Nutritional Quotient-elderly
OR	Odds ratio
PEW	Protein energy wasting

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12882-025-04006-5.

Supplementary Material 1.

Supplementary Material 2.

Acknowledgements

None

Authors' contributions

Conceptualization: TWY, and EB; methodology: YMK, DHK, and OYK; validation: YMK and YSK; formal analysis: YMK, DHK, and TWL; writing: TWY, DJP and EB.; supervision: OYK, DJP and EB; Funding Acquisition TWY, and EB.

Funding

This study was supported by the Lee Jung Ja research grant of Gyeongsang National University Hospital (LJJ-GNUH-2019–0006), and National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) [grant number: RS-2020-NR051028].

Data availability

Data availability The datasets generated and analysed during the current study are not publicly available due privacy concerns, but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study involved human participants who gave informed consent to participate in the study before participation and all research procedures were conducted in accordance with relevant guidelines and regulations, was approved by the Institutional Review Board of Gyeongsang National University Hospital (IRB No. 2019–03-014–001).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 14 May 2024 Accepted: 5 February 2025
Published online: 10 February 2025

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