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The Kidney Disease Quality of Life Cognitive Function Subscale and Cognitive Performance in Maintenance Hemodialysis Patients

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Abstract

Background—Cognitive impairment is common but often undiagnosed in patients with end-stage renal disease, in part reflecting limited validated and easily administered tools to assess cognitive function in dialysis patients. Accordingly, we assessed the utility of the Kidney Disease Quality of Life Cognitive Function (KDQOL-CF) scale in comparison to an extensive neuropsychological battery, building on a prior assessment of this potential cognitive screen.

Study Design—Cross-sectional cohort.

Setting & Participants—Maintenance hemodialysis patients at 6 Boston area dialysis units were administered an extensive neurocognitive battery and the KDQOL-CF at the beginning of a hemodialysis session.

Predictors—KDQOL-CF score, depression symptom burden, and demographic and clinical characteristics.

Outcomes—Neurocognitive performance classified into executive function and memory domains, determined using principal components analysis.

Measurements—Univariate and multivariable linear regression models adjusting for age, sex, race, and end-stage renal disease cause were used to evaluate the association between KDQOL-CF score and cognitive performance, and test metrics were determined for a KDQOL-CF cutoff score of 60 or less from a maximum score of 100.

Results—For 168 prevalent hemodialysis patients, KDQOL-CF score was 76 ± 19 and 40 (24%) had scores of 60 or less, consistent with self-identified worse cognitive performance. There was no significant correlation between KDQOL-CF score and either memory ($P = 0.2$ and $P = 0.3$) or

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executive function ($P = 0.1$ and $P = 0.4$) in univariate and multivariable models, respectively. There was a strong correlation between higher KDQOL-CF score and fewer depression symptoms ($P < 0.001$). Sensitivity of the KDQOL-CF was poor (range, 0.28–0.36), with modest specificity (range, 0.77–0.81) for identifying worse executive function and memory.

Limitations—Cross-sectional study, modest population size, and abbreviated gold-standard cognitive battery.

Conclusions—The KDQOL-CF is a poor determinant of neurocognitive performance in hemodialysis patients, with limited sensitivity. To assess cognitive impairment in hemodialysis patients, better screening tests are essential.

INDEX WORDS

Dialysis; dementia; cognitive impairment; screening; depression; quality of life

Cognitive impairment is common and often undiagnosed in people with end-stage renal disease (ESRD).[1–3] Cognitive impairment may accompany earlier stages of chronic kidney disease and appears increasingly prevalent with worse kidney function. [4–12] As many as two-thirds of dialysis patients may have moderate or severe cognitive impairment, [3, 13] a rate that is substantially higher than that in the age-matched general population.[14]

Cognitive impairment is not a benign comorbid condition in patients with kidney failure; rather, even mild cognitive impairment is associated with a significantly increased risk of mortality, hospitalization, and health care resource use.[15–17] Cognitive impairment also adversely affects patient decision making and patient self-care, potentially affecting individuals' abilities to participate fully in medical decisions, modify dietary habits, and adhere to complicated medication regimens.[18] Finally, cognitive impairment is associated with worse quality of life and emotional well-being.[16, 19–23] Given these factors, screening for cognitive impairment in patients with ESRD is important. However, presently, there are no well-validated neurocognitive tests routinely performed in the ESRD population, potentially reflecting the complex nature of cognitive impairment patterns in these patients, for whom executive functions (eg, the ability to plan and manage items such as medication regimens) appear more affected than memory domains.[8, 11, 24]

Quality-of-life ascertainment in dialysis patients is federally mandated in the United States by the Conditions for Coverage for ESRD Facilities 2008 final rule,[25] and the instrument suggested for this purpose by the Centers for Medicare & Medicaid Services is the Kidney Disease Quality of Life (KDQOL)-36 assessment survey.[26] The KDQOL is a self-administered questionnaire consisting of a generic core derived from the Medical Outcomes Study 36-Item Short Form Health Survey and additional kidney disease-targeted subscales, including questions addressing cognitive function.[26, 27] As the KDQOL becomes increasingly used, it is likely that the components of this instrument will be applied more frequently in clinical diagnoses and decision making, with the KDQOL–Cognitive Function (KDQOL-CF) one of these components.

Kurella Tamura et al[28] evaluated the correlation between answers on 3 questions on the KDQOL that address cognition, dubbed the KDQOL-CF subscale, and scores on a separately administered Modified Mini-Mental State Examination (3MS) in 157 individuals, 79 with ESRD and 78 with chronic kidney disease stages 3–4. This study showed a modest correlation between lower summary KDQOL-CF score and lower 3MS score. Defining global cognitive impairment as a 3MS score less than 80, a summary score of 60 or lower on the KDQOL-CF accurately classified 76% of individuals with 81% specificity and 52%

sensitivity, and the authors concluded that the KDQOL-CF is a valid screening instrument for estimating cognitive function in patients with chronic kidney disease and ESRD.[28]

Although a widely used global test of cognition, the 3MS focuses on memory and is not optimal for assessing other cognitive domains,[29] specifically domains that encompass executive functioning and processing speed, both of which are more likely to be impaired in individuals with kidney disease and/or small-vessel cerebrovascular disease.[30–32] Accordingly, this study aims to reassess the utility of the KDQOL-CF scale for identifying cognitive impairment in hemodialysis patients using an extensive neuropsychological battery that evaluates multiple cognitive domains.

METHODS

Participants

Patients receiving long-term in-center hemodialysis at 6 Boston, MA, area hemodialysis units (5 Dialysis Clinic Inc [DCI] facilities and St. Elizabeth's Medical Center) were evaluated for participation in the present study. Eligible participants were fluent in English and had sufficient visual and hearing acuity to complete cognitive tests. Exclusion criteria included advanced dementia or confusion (as defined by provider testimony, medical chart review, or Mini-Mental State Examination score ≤10), non–access-related acute hospitalization within 1 month, receipt of maintenance hemodialysis for less than 1 month, and single-pool Kt/V <1.0. Demographic data were obtained through personal history, dialysis and hospital charts, and the DCI and St. Elizabeth's databases. The Tufts Medical Center Institutional Review Board approved the study, and all participants signed informed consent and research authorization forms.

Neuropsychiatric Evaluation

Participants were administered a battery of cognitive tests by research assistants trained by the study neuropsychologist (T.S.). To ensure quality and inter-rater reliability, research assistants were re-evaluated by the study neuropsychologist at 3- to 6-month intervals through either mock testing sessions or overseeing actual cognitive test administration. To limit participant fatigue effects from the hemodialysis procedure, testing was completed during the first hour of dialysis. Testing was deferred if participants presented to dialysis feeling poorly that day and would be aborted for acute medical events occurring during the testing period (although this did not occur). The neuropsychiatric battery included validated and commonly used cognitive tests that possess high inter- and intrarater reliability, with many of these tests having established age, sex, and/or education-matched normative scores (Table 1).[33–38] This cognitive battery explores a wide range of cognitive functions and domains, including global function, supraspan learning, auditory retention, visual retention, attention/mental processing speed, visual construction/fluid reasoning, and motor speed, spanning memory, and executive functioning domains.

Participants self-completed the Center for Epidemiological Studies Depression Scale (CES-D)[39] and the KDQOL-CF (Table 2). Each of the 3 KDQOL-CF questions are answered using a qualitative 6-point scale; the KDQOL-CF score was calculated as 100 × (sum/15), where sum is the total score across the 3 questions for each participant, such that the score could range from 0–100, with the maximum score of 100 awarded to those who self-identified as having the least cognitive difficulties.[28]

Study Outcomes

The primary study outcomes were neurocognitive performance quantified using principal components analysis.[40] For 15 individuals who were missing results on one cognitive test

(or 2 results if derived from the same test), single-item imputation was performed using multivariable linear regression models based on performance on other tests in the cognitive battery. These imputation results were incorporated to derive the principal components analysis but were not used for evaluating performance on individual cognitive tests. Principal component analysis with varimax rotation was used to derive composite scores for separate cognitive domains. Principal component analysis is used to group results of multiple tests into fewer interrelated domains, minimizing the influence of any single test while emphasizing consistent performance on tests that assess similar cognitive functions. After application of this data-reduction technique, 2 principal components with eigenvalues greater than 1 were obtained. The first component, with explained variance of 3.3 after rotation, consisted primarily of the Trail Making Tests A and B, Block Design, Digit Symbol-Coding, Digit Span, Mental Alternations, and COWAT (Controlled OralWord Association Test) tasks and was considered to reflect executive functioning, attention, and processing speed (hereafter referred to as executive function). The second component, with explained variance of 3.5 after rotation, consisted primarily of the Word List Learning Recall and Recognition tasks, also modestly incorporated Digit-Symbol Coding and the COWAT tasks (hereafter referred to as memory).

Statistical Analyses

Of eligible dialysis patients, those who did and did not consent were compared using χ^2 tests, *t* tests, and analysis of variance, as appropriate. Baseline characteristics of participants were examined by quartiles of KDQOL-CF score. Simple linear regression was used to determine the association between KDQOL-CF score and each principal component, with multivariable models further adjusting for age, sex, race, education, and cause of kidney failure. Similarly, in secondary analyses, simple and multivariable linear regression models examined the association between KDQOL-CF score and raw score on each of the individual tests in the cognitive battery. Analyses with Trails B performance as an outcome used Tobit regression to censor for failure to complete the task with the allotted 5 minutes.[41] Because prior stroke may identify a person at higher baseline risk of poor cognitive performance, we performed sensitivity analyses examining the association between KDQOL-CF score and each principal component in individuals without a history of stroke.

To explore the utility of the KDQOL-CF as a diagnostic test for identifying neurocognitive deficits, sensitivity, specificity, and positive (PPV) and negative predictive values (NPV) for a KDQOL-CF cutoff score of 60 were calculated for both the executive function and memory components derived from principal component analysis, using principal component scores ≥0.5 standard deviations (SDs) and ≥1.0 SD less than the study sample mean to define cognitive impairment. The cutoff score of 60 on the KDQOL-CF reflects the findings of Kurella et al[28] that this value was associated with the best receiver operating characteristic (ROC) curve characteristics. We further investigated the reproducibility of this cutoff using ROC curves that varied the cutoffs on the KDQOL-CF score from 40–80 in 5-point increments, and then varied the cutoffs on executive and memory function from 0.25–1.5 SD less than the study sample mean. Similarly, sensitivity, specificity, PPV, and NPV were calculated for each individual test after standardizing results on individual cognitive tests to population norms. For cognitive tests that are part of the Wechsler Adult Intelligence Scale, results were standardized for age, with population norms of 10 ± 3; accordingly, impaiment was defined as a scaled score less than 7.[37] For the Trail Making Tasks, age-, sex-, and education-specific T scores were derived, with population norms of 50 ± 10[35]; accordingly, impairment was defined as a scaled score less than 40. For the mental alternations task and COWAT, normal values were extrapolated from published data, with impairment defined as a score less than 15 on the mental alternations task[36,42] and less than the age- and education-adjusted 25th percentile fluency scores for the COWAT.[43]

All statistical analyses were performed using SAS, version 9.2 (SAS Institute, www.sas.com), except regression imputation, which was performed using the transcan function in Hmisc library of the R package (www.r-project.org). All statistical tests were 2 sided and differences were considered statistically significant at $P < 0.05$.

RESULTS

Of 487 patients meeting eligibility criteria, 324 (66.5%) agreed to participate in the study, 168 (51.9%) of whom joined the study after addition of the KDQOL-CF to the cognitive battery. There were 144 participants with complete cognitive assessments. Participants who provided consent were similar to those who did not across characteristics, including age, race, sex, primary cause of kidney disease, and cardiovascular comorbid conditions (results not shown), whereas those who completed the KDQOL-CF were slightly younger, more often were African American, and had lower rates of coronary artery disease. Mean age of enrolled participants who completed the KDQOL-CF was 62 ± 17 years; 51% were men, 30% were black, 90% were high school graduates, and 33% had diabetes causing ESRD. Demographic and clinical characteristics were similar across quartiles of KDQOL-CF score (Table 3).

Mean KDQOL-CF score was 76 ± 19 (maximum, 100), and 40 (24%) participants had scores of 60 or lower. Cognitive test results are listed in Table 4. In linear regression models, there was no significant correlation between KDQOL-CF score and either executive function component score (β = 0.13 [95% confidence interval (CI), −0.03 to 0.28; $P = 0.1$] and β = 0.05 [95% CI, −0.08 to 0.19; $P = 0.4$] for univariate and multivariable models, respectively) or the memory component score (β = 0.12 [95% CI, −0.05 to 0.28; $P = 0.2$] and β = 0.07 [95% CI, −0.07 to 0.22; $P = 0.3$] for univariate and multivariable models, respectively; Table 5). Similarly, associations were not significant for most individual subtests in the neurocognitive battery. However, in analyses adjusted for age, sex, race, education, and cause of kidney failure, statistically significant associations included a modest positive correlation with immediate recall ($P = 0.04$; Table 5). In multivariable analyses, there was a very strong positive correlation between KDQOL-CF score and CES-D total score ($P < 0.001$; Table 5), such that individuals self-identifying as having better cognitive function had fewer depressive symptoms. There were 137 participants without a history of stroke. The relationship between KDQOL-CF score and cognitive function was similar in this subgroup, with β values of 0.09 (95% CI, −0.05 to 0.24; $P = 0.2$) and 0.11 (95% CI, −0.05 to 0.28; $P = 0.2$) for executive function and memory component scores, respectively, in adjusted analyses (data not shown).

We also examined the sensitivity, specificity, PPV, and NPV of KDQOL-CF score. Using a cutoff score of 60 on the KDQOL-CF, sensitivity generally was poor, with modest specificity (range, 0.75–0.85) and PPV and NPV that varied by cognitive test (Table 6). Varying cutoff scores for the KDQOL-CF and executive and memory factors did not result in improvement in the areas under the ROC curve (AUROCs), with noAUROC significantly differing from 0.500 for memory, and only a cutoff of 0.5 SD less than the mean and KDQOL-CF score less than 60 differing from an AUROC of 0.500 for executive function. Although the CES-D had the most statistically significant association with KDQOL-CF score in regression models and had the only AUROC higher than 0.6, sensitivity remained poor for this test when using previously accepted CES-D cutoffs used to screen for depression. Of note, in models evaluating principal component scores that were adjusted for age, education, sex, race, and cause of ESRD in addition to KDQOL-CF score, AUROCs for the executive function component were 0.755 and 0.795 for 0.5 and 1 SD less than the population mean, respectively, and for the memory component, were 0.763 and 0.756, respectively.

DISCUSSION

In this study, we assessed the utility of the KDQOL-CF in predicting neurocognitive performance in dialysis patients compared with a more detailed cognitive battery and showed that the KDQOL-CF is a limited instrument for accurately assessing cognitive function. The null finding for the executive functioning component is particularly notable because prior work by our group and others suggests that executive functioning is the cognitive domain most commonly affected in kidney disease and dialysis patients.[8, 11, 32] Bearing in mind that the KDQOL-CF currently is the only screening test for cognitive impairment that dialysis centers are required to administer, our findings suggest that to better screen for cognitive impairment, different tests will be required.

The KDQOL-CF relies on self-assessment to identify cognitive difficulties. Although a self-administered screening test offers the benefit of brevity and parsimony with resources, this format is limited by the possibility that individuals with cognitive difficulties are unable to recognize their own impairments. The present study reinforces the literature for the general population, which notes that subjective memory concerns are related inconsistently to prevalent cognitive impairment, but often are associated with depression.[44] Accordingly, the present study suggests that we should cautiously interpret the role of the KDQOL-CF for identifying dialysis patients with cognitive impairment. Given the very poor sensitivity noted in our study and the poor sensitivity noted in the study by Kurella et al, one can conclude that a score higher than 60 on KDQOL-CF is unable to show that a particular patient's cognitive function is intact.[28] Both the present study and the study by Kurella et al showed only modest specificity, suggesting that a low score on the KDQOL-CF is often but not always associated with cognitive impairment. A possible explanation for the far worse sensitivity in our study is the use of a more detailed cognitive battery that focuses on both executive function domains and memory domains rather than the 3MS, which is oriented more toward memory.[10] However, in concordance with a finding by Kurella Tamura et al, we also noted a significant correlation between the KDQOL-CF score and depressive symptoms as identified using the CES-D.[28] Although this may represent an association between cognitive function and depressive symptoms,[16, 19] it also could indicate that the KDQOL-CF serves as a proxy for either depression or symptoms of depression. This is not surprising because several KDQOL-CF questions are similar to CES-D questions, such as "I could not get 'going'" and "I had trouble keeping my mind on what I was doing."

Dialysis patients are faced with complex medical tasks, including diet and binder management, fluid restrictions, and balancing complex medication regimens. However, many may lack the cognitive skills necessary to adequately juggle these many requirements, reflecting the finding that cognitive impairment is common and often undiagnosed in dialysis patients. Given these factors, it is not surprising that cognitive impairment in dialysis patients is associated with increased mortality and resource utilization, as well as decreased quality of life, making the establishment of a well-validated screening test both clinically and academically important in this population. Presently, a wide range of screening tests for cognitive impairment and dementia exists for the general population; however, none has been validated in patients with kidney disease and few have both high sensitivity and specificity, particularly when it comes to evaluating impairment in executive function, the domain more often associated with small-vessel cerebrovascular disease.[45–46] Ultimately, screening for cognitive impairment in dialysis patients may be enhanced by using tasks that better evaluate executive function, attention, and processing speed. However, implementation of these tests would require either the availability of technology such as tablet computers that can be used for this task or training dialysis unit personnel to administer several brief neurocognitive tests that better assess these cognitive domains without imposing substantial time or cost burdens.

There are several limitations to this study. First, the cognitive battery used as a gold standard in this study consisted of excerpts from established neurocognitive examinations, not one cohesive test to specifically examine certain domains. However, the method of principal components analysis, a common technique in neurocognitive studies,[40, 47] was used and subsequent comparison with individual subtests suggests that analyses with each component are sound. Additionally, a fairly parsimonious model that included characteristics typically associated with both executive function and memory showed fairly good fit, with C statistics in the 0.75–0.80 range, suggesting that the cognitive battery likely provides at least some reasonable measure of cognitive performance. Second, the use of principal components analysis for data reduction may be less appropriate in studies of diagnostic accuracy because the concept of poor performance is based entirely on this cohort's distribution of cognitive test scores rather than a gold-standard definition of cognitive impairment or population normative values, such that weighting of the executive and memory factors could be different in different populations. However, we believe it is important to include the principal components analyses because they show the ability to predict cognitive performance using demographic and clinical characteristics, as well as permitting a summary view of cognitive performance across executive function and memory domains. Third, cognitive tests were carried out during the dialysis session. Although this potentially could interfere with cognitive test performance,[48] assessment in this setting is important given that the practical administration of cognitive assessment tools would involve administration in the dialysis unit and most interactions between dialysis patients and staff, including physicians, nurses, nutritionists, and social workers, occur during the dialysis session. Fourth, we did not recruit patients with overt dementia or nonelective hospitalization within the past month, potentially resulting in better cognitive performance than expected for the wider hemodialysis population. This may limit generalizability, but these results should still be applicable to stable dialysis patients. Finally, we had a modest sample size for the individual test analysis (n = 168). However, by using principal components analysis, the domain-specific information from each subtest was maximized.

This study also has several strengths. First, our cognitive battery includes a wide range of tests that encompass a broad spectrum of cognitive domains, facilitating identification of impairments in domains such as executive functioning. Second, the statistical method of principal components analysis allowed us to account for within-patient between-test variability and reduces concerns with multiple testing.[47] Third, we had few exclusion criteria, with those refusing consent having demographics similar to those consenting, which made our cohort relatively generalizable. Our participants had characteristics and causes of ESRD similar to those in the prevalent US dialysis population as determined by the US Renal Data System, albeit with a lower proportion of individuals with diabetes.[49]

In summary, we show that the KDQOL-CF is a poor determinant of neurocognitive performance in hemodialysis patients, with very limited sensitivity for identifying individuals with poor performance on neurocognitive tests, using a cutoff score of 60 as well as limited overall test performance when examined on a continuous scale. Given the very high prevalence of cognitive impairment in dialysis patients, the substantial adverse consequences of cognitive impairment, and the absence of any well-validated screening tests in the dialysis population, future research directed at developing appropriate screening tests for this population is essential. Potential screening tests with more extensive ascertainment of executive functioning, such as the Montreal Cognitive Assessment[50] or the Saint Louis University Mental Status,[51] are possible instruments for screening individuals when memory is expected to be disproportionately unaffected, but these tests require validation in a dialysis population.

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Table 1

Cognitive Tests Used in the Neurocognitive Battery, Categorized by the Primary Cognitive Domain Evaluated

Function Assessed	Cognitive Test	Scoring	Test Details
Cognitive screen	Mini-Mental State Examination	No. correct	30-point questionnaire that samples abilities such as arithmetic, memory, and orientation
Intelligence	North American Adult Reading Test	128.7 – (0.89 × no. of errors)	Estimation of verbal intelligence quotient that requires participants to read a list of 61 words out loud
Supraspan Learning & Word Recall	Immediate Recall[a] Delayed Recall[a] Percent Retention[a] Delayed Recognition[a]	Total initially correct Total no. recalled after delay % recall after delay No. of correctly identified Words	Assessment of memory in which a list of 12 words is presented during 4 trials, and retention of these words is tested after a delay of 25–35 min. Calculated scores include immediate recall (words recalled during the 4 trials), delayed recall (words from trial 4 recalled after a delay), percent retention ([delayed recall/trial 4 of immediate recall] × 100), and delayed recognition
Visual Construction & Fluid Reasoning	Block Design[b]	No. completed weighted for time	Participants are required to reproduce depicted patterns using a set of colored blocks
Working Memory	Digit Span[b]	No. completed × 0.5	Participants recite strings of numbers forward and backward, beginning with two 2-digit strings
Attention, Mental Processing Speed, & Executive Function	Digit Symbol-Coding[b]	No. of copied symbols in 2 min	Symbols are decoded by matching a given symbol to a digit provided in an answer key
	Trail Making Test A	Time to completion	“Connect-the-dots” for a consecutive number sequence from 1–25
	Trail Making Test B	Time to completion	“Connect-the-dots” alternating between numbers (1–13) and letters (A-L)
	Mental Alternations	Total correct no.	Participants are asked to alternate between sequential numbers and letters aloud
	COWAT (animals and supermarket items)	No. of correct examples	Participants asked to name as many animals and supermarket items as they can in 1 min each

Abbreviation: COWAT, Controlled Oral Word Association Test.

[a]Derived from the Word List Learning subtest of the Wechsler Memory Scale-III.

[b]Derived from the Weschler Adult Intelligence Scale.

Table 2

The KDQOL Cognitive Function Questions and Scoring

How Much of the Time During the Past 4 Weeks…	None	A Little	Some	A Good Bit	Most	All
…did you have difficulty concentrating or thinking?	5	4	3	2	1	0
…did you react slowly to things that were said or done?	5	4	3	2	1	0
…did you become confused?	5	4	3	2	1	0

Note: The KDQOL-Cognitive Function score was calculated as 100 × (sum/15), where sum is the total score across the 3 questions for each participant, such that the score could range from 0–100, with the maximum score of 100 awarded to those who self-identified as having the least cognitive difficulties. In calculating sensitivity and specificity, individuals scoring 9 or lower (summed score of 60) were considered to have identified themselves as impaired.

Abbreviation: KDQOL, Kidney Disease Quality of Life.

Table 3

Baseline Characteristics of the Study Population, Categorized by Quartile of KDQOL-CF Score

	KDQOL-CF Quartile					
	1 (n = 40; 24%)	**2 (n = 40; 24%)**	**3 (n = 41; 24%)**	**4 (n = 47; 28%)**	**Total (n = 168)**	***P***
KDQOL-CF score[a]	50 ± 13 (13–60)	71 ± 3 (67–73)	84 ± 3 (80–87)	98 ± 3 (93–100)	76 ± 19 (13–100)	<0.001
Age (y)	62 ± 15	63 ± 17	61 ± 15	61 ± 19	62 ± 17	0.9
Male sex (%)	58	53	51	43	51	0.2
Black race (%)	30	33	22	34	30	0.9
Educational level (%)						0.2
<12th grade	18	3	10	9	10	
High school graduate	48	55	39	40	45	
≥2 y college	35	43	51	51	45	
Dialysis duration (mo)	33 (12–48)	29 (15–62)	29 (13–39)	32 (16–49)	32 (13–49)	0.7
Cause of ESRD (%)						0.6
Diabetes	33	33	39	30	33	
Hypertension	15	25	12	26	20	
Glomerulonephritis	8	20	29	15	18	
Other	20	10	7	15	13	
Unknown	25	13	12	15	16	
Smoking status (%)						0.5
Never	30	45	41	45	41	
Former	60	41	51	47	50	
Current	10	13	7	9	10	
Medical history (%)						
Stroke	13	23	10	28	18	0.2
CAD	25	40	29	34	32	0.6
PVD	18	25	22	11	18	0.3
Hypertension	85	95	93	94	92	0.2
Diabetes	58	43	49	47	49	0.5
Heart failure	45	35	34	28	35	0.1
Examination and laboratory results						

	KDQOL-CF Quartile					
	1 (n = 40; 24%)	**2 (n = 40; 24%)**	**3 (n = 41; 24%)**	**4 (n = 47; 28%)**	**Total (n = 168)**	***P***
Systolic BP (mm Hg)	133 ± 18	140 ± 24	142 ± 20	143 ± 23	140 ± 22	0.03
Diastolic BP (mm Hg)	71 ± 12	71 ± 14	73 ± 13	75 ± 15	73 ± 13	0.3
BMI (kg/m^2)	30 ± 7	28 ± 6	30 ± 9	29 ± 8	29 ± 8	0.6
Single-pool Kt/V	1.55 ± 0.30	1.53 ± 0.20	1.49 ± 0.21	1.56 ± 0.27	1.53 ± 0.25	0.7
Albumin (g/dL)	3.8 ± 0.4	3.8 ± 0.4	3.8 ± 0.3	3.8 ± 0.4	3.8 ± 0.4	0.6
Phosphorus (mg/dL)	5.3 ± 1.6	5.7 ± 1.6	6.3 ± 1.5	5.6 ± 1.4	5.7 ± 1.6	0.09

Note: Categorical data presented as percentage; continuous variables, as mean ± standard deviation or median (25th–75th percentile). Individuals in quartile 1 are those with the worst self-assessment of performance based on KDQOL-CF score, whereas those in quartile 4 are the best performers. For 22 individuals (receiving dialysis at a non–Dialysis Clinics Inc facility), blood pressure results are from a single dialysis session rather than a monthly average. Conversion factors for units: creatinine in mg/dL to mol/L, ×88.4; albumin in g/dL to g/L, ×10; phosphorus in mg/dL to mmol/L, ×0.3229.

Abbreviations: BP, blood pressure; BMI, body mass index; CAD, coronary artery disease; ESRD, end-stage renal disease; KDQOL-CF, Kidney Disease Quality of Life-Cognitive Function; PVD, peripheral vascular disease.

[a]Range is provided in parentheses.

Table 4

Neurocognitive Test Performance Stratified by Quartile of KDQOL-CF

	KDQOL-CF Quartile					
	1 (n = 40; 24%)	**2 (n = 40; 24%)**	**3 (n = 41; 24%)**	**4 (n = 47; 28%)**	**Total (n = 168)**	**Trend *P***
Executive Factor	−0.25 ± 0.85 (35)	0.07 ± 0.84 (34)	0.19 ± 0.99 (35)	0.00 ± 1.00 (40)	0.00 ± 0.93 (144)	0.2
Memory Factor	−0.16 ± 0.91 (35)	0.07 ± 0.94 (34)	−0.13 ± 0.84 (35)	0.19 ± 1.11 (40)	0.00 ± 0.96 (144)	0.2
MMSE	26.0 ± 3.0 (40)	26.2 ± 2.6 (40)	27.0 ± 2.6 (41)	26.6 ± 2.9 (47)	26.4 ± 2.8 (168)	0.2
Verbal IQ	100 ± 12 (39)	103 ± 11 (38)	105 ± 11 (41)	104 ± 13 (46)	103 ± 12 (164)	0.1
Delayed Recall	4.4 ± 2.5 (38)	4.9 ± 2.6 (39)	4.7 ± 2.5 (41)	5.4 ± 3.1 (47)	4.9 ± 2.7 (165)	0.2
Short Delay	4.8 ± 2.7 (39)	5.3 ± 2.8 (39)	4.5 ± 2.6 (41)	5.7 ± 3.3 (47)	5.1 ± 2.9 (166)	0.3
Immediate Recall	23 ± 7 (39)	24 ± 7 (39)	24 ± 7 (41)	26 ± 8 (47)	24 ± 7 (166)	0.06
Percent Retention	57 ± 26 (38)	65 ± 26 (39)	57 ± 26 (41)	61 ± 28 (47)	60 ± 27 (165)	0.7
Recognition	20.8 ± 2.4 (38)	20.9 ± 2.4 (39)	20.9 ± 2.6 (41)	20.9 ± 2.9 (47)	20.9 ± 2.6 (165)	0.6
Block Design	24 ± 10 (40)	26 ± 11 (38)	27 ± 10 (39)	24 ± 11 (45)	25 ± 10 (162)	0.9
Digit Symbol	34 ± 13 (35)	45 ± 17 (33)	43 ± 18 (33)	45 ± 18 (35)	42 ± 17 (136)	0.02
Digit Span	14 ± 3 (38)	15 ± 3 (39)	17 ± 4 (41)	15 ± 4 (47)	15 ± 4 (165)	0.03
Trail Making Test A	64 ± 27 (37)	49 ± 20 (35)	66 ± 63 (35)	72 ± 51 (39)	63 ± 44 (146)	0.7
Trail Making Test B[a]	155 ± 56 (28)	130 ± 53 (28)	132 ± 62 (29)	127 ± 76 (29)	136 ± 63 (114)	0.01
Completed Trail Making Test B[b]	9 (24)	7 (20)	6 (17)	10 (26)	32 (22)	0.9
COWAT animal	14.6 ± 5.5 (40)	15.2 ± 4.8 (39)	15.6 ± 5.4 (41)	15.7 ± 6.8 (47)	15.3 ± 5.7 (167)	0.5
COWAT market	20.1 ± 5.5 (40)	20.2 ± 6.0 (40)	20.7 ± 7.2 (41)	21.4 ± 6.9 (47)	20.6 ± 6.4 (168)	0.3
Mental Alternations	19.3 ± 7.3 (39)	19.2 ± 7.0 (40)	20.7 ± 7.9 (41)	20.8 ± 8.2 (47)	20.0 ± 7.6 (167)	0.4
CES-D total	15.8 ± 8.6 (39)	12.8 ± 6.1 (40)	11.5 ± 8.0 (41)	7.9 ± 6.2 (46)	11.8 ± 7.7 (166)	<0.001

Note: Unless otherwise indicated, data are presented as mean ± standard deviation, with the number performing each test in parentheses.

Abbreviations: CES-D, Center for Epidemiologic Studies Depression; COWAT, Controlled Oral Word Association Test; KDQOL-CF, Kidney Disease Quality of Life-Cognitive Function; MMSE, Mini-Mental State Examination.

[a]Restricted to those completing only.

[b]Data shown are number (percentage).

Table 5

Univariate and Multivariable Associations Between KDQOL-CF Score and Neurocognitive Performance

		Univariate		Multivariable Adjusted	
Neurocognitive Assessment	**No.**	**β (95% CI)**	***P***	**β (95% CI)**	***P***
Executive Factor	144	0.13 (−0.03 to 0.28)	0.1	0.05 (−0.08 to 0.19)	0.4
Memory Factor	144	0.12 (−0.05 to 0.28)	0.2	0.07 (−0.07 to 0.22)	0.3
MMSE	168	0.23 (−0.19 to 0.66)	0.3	0.09 (−0.31 to 0.49)	0.6
Delayed Recall	165	0.29 (−0.13 to 0.72)	0.2	0.21 (−0.18 to 0.59)	0.3
Short Delay	166	0.27 (−0.18 to 0.72)	0.2	0.17 (−0.23 to 0.57)	0.4
Immediate Recall	166	1.27 (0.21 to 2.33)	0.02	0.94 (0.06 to 1.82)	0.04
Percent Retention	165	0.70 (−3.50 to 4.91)	0.7	0.40 (−3.78 to 4.58)	0.9
Recognition	165	0.10 (−0.30 to 0.51)	0.6	0.04 (−0.34 to 0.42)	0.9
Block Design	162	0.51 (−1.09 to 2.11)	0.5	−0.08 (−1.38 to 1.22)	0.9
Digit Symbol	136	3.93 (0.98 to 6.87)	0.009	1.58 (−0.74 to 3.90)	0.2
Digit Total	165	0.51 (−0.10 to 1.12)	0.1	0.48 (−0.12 to 1.08)	0.1
Trail Making Test A	146	3.95 (−3.27 to 11.16)	0.3	6.62 (−0.45 to 13.70)	0.07
Trail Making Test B	146	−11.1 (−29.25 to 7.02)	0.2	−4.19 (−19.95 to 11.57)	0.6
COWAT market	168	0.53 (−0.45 to 1.51)	0.3	0.42 (−0.53 to 1.37)	0.4
COWAT animal	167	0.47 (−0.40 to 1.35)	0.3	0.33 (−0.48 to 1.14)	0.4
Mental Alternations	167	0.74 (−0.43 to 1.90)	0.2	0.67 (−0.39 to 1.74)	0.2
CES-D total	166	−2.66 (−3.81 to −1.52)	<0.001	−2.55 (−3.72 to −1.37)	<0.001

Note: Multivariable models are adjusted for age, sex, race, education, and cause of kidney failure. For all neurocognitive assessments, higher values are consistent with better performance, except Trail Making Tests A/B and the CES-D, for which lower scores are better. Higher values on the KDQOL-CF are consistent with better self-identified cognitive performance. All β coefficients are per 1-standard deviation increase in KDQOL-CF score. Trail Making Test B models used Tobit regression.

Abbreviations: CI, confidence interval; COWAT, Controlled Oral Word Association Test. CES-D, Center for Epidemiologic Studies-Depression; KDQOL-CF, Kidney Disease Quality of Life-Cognitive Function; MMSE, Mini-Mental State Examination.

Table 6

Predictive Ability of the KDQOL-CF for Composite and Individual Cognitive Measures

Test/Factor	Metric	Below Metric (%)[a]	Sensitivity	Specificity	PPV	NPV	AUROC[b]
Executive Factor	≥0.5 SD below this sample mean	31	0.36	0.81	0.46	0.73	0.571
Executive Factor	≥1.0 SD below this sample mean	15	0.33	0.77	0.20	0.87	0.507
Memory Factor	≥0.5 SD below this sample mean	37	0.28	0.78	0.43	0.65	0.537
Memory Factor	≥1.0 SD below this sample mean	15	0.33	0.77	0.20	0.87	0.557
MMSE	Score <24	15	0.27	0.77	0.18	0.85	0.507
Recall[c]	≥1.0 SD below general population norm	54	0.27	0.81	0.62	0.49	0.562
Delayed Recall[c]	≥1.0 SD below general population norm	8	0.15	0.76	0.05	0.91	0.552
Recognition[c]	≥1.0 SD below general population norm	26	0.23	0.77	0.26	0.74	0.552
Block Design[c]	≥1.0 SD below general population norm	37	0.27	0.76	0.40	0.64	0.543
Digit Symbol[c]	≥1.0 SD below general population norm	59	0.34	0.85	0.77	0.47	0.592
Trail Making Test A[d]	≥1.0 SD below general population norm	66	0.31	0.84	0.78	0.39	0.509
Trail Making Test B[d]	≥1.0 SD below general population norm	63	0.29	0.80	0.70	0.40	0.565
Digit Span[c]	≥1.0 SD below general population norm	24	0.38	0.82	0.39	0.80	0.573
COWAT[e]	Lowest quartile of general population	54	0.26	0.78	0.58	0.47	0.526
Mental Alternations	<15 alternations	26	0.23	0.77	0.26	0.74	0.529
CES-D	Score >15	30	0.37	0.82	0.46	0.76	0.671

Note: Below Metric (%) indicates the proportion of the study sample with cognitive performance below the metric for the individual test. For example, 30% of the population had a CES-D score above 15.

Abbreviations: AUROC, area under receiver operating characteristic curve; CES-D, Center for Epidemiologic Studies–Depression; COWAT, controlled oral word association test; KDQOL-CF, Kidney Disease Quality of Life–Cognitive Function; MMSE, Mini-Mental State Examination; NPV, negative predictive value; PPV, positive predictive value; SD, standard deviation.

[a] Indicates the proportion of dialysis patients with scaled scores (when appropriate) performing below the metric score indicated in the table.

[b] Calculated using KDQOL-CF on the continuous scale.

[c] Standardized for age.

[d] Standardized for age, sex, and education.

[e] Standardized for age and education.