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Screening for cognitive symptoms in dialysis patients with an extended version of Kidney Disease Quality of Life Cognitive Function subscale (KDQOL-CF): a validation study

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Abstract

Background Cognitive impairment and cognitive complaints are highly prevalent in haemodialysis patients and are associated with adverse health outcomes. Currently, there is no established guideline on cognitive screening in this population. Although neuropsychological tests are the gold standard measure of cognition, they are time-consuming and require trained personnel. The Kidney Disease Quality of Life Cognitive Function subscale (KDQOL-CF), a self-administered questionnaire with only three items, may be a feasible alternative for busy renal settings. In this study, we validated an extended version of KDQOL-CF by including an additional memory item (i.e., "How much of the time during the past four weeks did you have memory difficulties?") to improve its ability to capture memory impairments that are common in dialysis patients but missing in the original scale.

Methods A total of 268 haemodialysis patients treated in 10 dialysis centres in Singapore completed the extended KDQOL-CF and gold standard measures of objective cognition (Montreal Cognitive Assessment) and subjective cognition (Patient's Assessment of Own Functioning Inventory). Patients also self-reported their functional impairment and treatment nonadherence. Statistical analyses were performed to determine the factor structure and psychometric properties of the extended KDQOL-CF. Receiver operating characteristic curve analyses were conducted to determine the diagnostic ability of the extended KDQOL-CF in identifying objective cognitive impairments and subjective cognitive complaints. Additionally, we examined associations between the extended KDQOL-CF and patients' self-reported functional impairment and treatment nonadherence.

Results The extended KDQOL-CF can be explained by a one-factor model and has good internal consistency and convergent validity. Receiver operating characteristic curve analysis provided support for the diagnostic accuracy of the extended KDQOL-CF in identifying objective cognitive impairments (area under curve = 60.9%) and subjective cognitive complaints (area under curve = 76.2%). The extended KDQOL-CF also performed better than the original KDQOL-CF in predicting functional impairment and treatment nonadherence in the recruited patients.

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Conclusions The extended KDQOL-CF may be used as a first-step cognitive screening tool in dialysis settings to offer a gateway for further diagnostic evaluation and preventive or rehabilitative programs.

Keywords Cognitive impairment, Subjective cognitive complaint, Haemodialysis, End-stage renal disease, Screening

Introduction

Cognitive impairments (CIs) are very common in haemodialysis (HD) patients. Studies using neuropsychological tests have found that less than 30% of HD patients had intact cognitive function, and more than half had moderate to severe CIs [1, 2]. Other studies have assessed patient-perceived CIs, or subjective cognitive complaints (SCCs), that were found to be present in more than two thirds of HD patients [3]. Both objective and subjective CIs have been associated with adverse health outcomes including functional impairment, treatment nonadherence, poor quality of life, hospitalisation, and mortality [3–9]. However, CIs in HD patients are poorly recognised; less than 15% of those with CIs had chart documentation [2, 6].

Identifying objective CIs in HD patients is pivotal as it enables healthcare providers to establish diagnosis, initiate cognitive rehabilitation or compensatory strategies, and may allow for advance care planning as appropriate. Although research on the effectiveness of interventions targeting CIs in HD patients is scarce, several strategies have shown promising results. In particular, a recent randomised controlled trial showed that a 12-week combined intradialytic cycling and cognitive training program significantly enhances cognitive function among HD patients [10]. There is also evidence that certain renal replacement modalities result in better cognitive outcomes. Kidney transplantation significantly improves cognitive function in dialysis patients [11]. Cooled dialysis offers cognitive benefits including better systemic haemodynamic stability, less alteration in cerebral white matter, and less cerebral ischaemic incidents during HD [1, 12, 13]. Interventions aimed at improving toxin clearance, such as nocturnal daily HD [14], and haemodiafiltration in the recent CONVINCE trial [15], have also demonstrated cognitive advantages over conventional thrice-weekly HD.

Assessing SCCs is equally important because they reflect patients' experienced cognitive difficulties in everyday life that interfere with functional capacity and treatment adherence [4, 5, 9]. Also, SCCs are now regarded as a prodromal marker of future progression to mild CIs and dementia, which may offer a gateway to further neuropsychological evaluation or preventive programs [16, 17]. To date, research in the context of chronic kidney disease has primarily focused on objective CIs and neuropsychological performance, with SCCs typically thought to be unreliable or inaccurate.

Several studies have validated the Montreal Cognitive Assessment (MoCA), with results showing variable sensitivity and specificity for identifying objective CIs in HD patients [18–20]. There is a growing consensus that MoCA is a screening tool superior to other objective measures such as the Mini-Mental State Examination (MMSE) because of its inclusion of executive function, a domain predominantly impaired in HD patients [21]. Despite mounting evidence supporting the use of MoCA in this population [18–21], its implementation in real-world dialysis settings as a first-step screener can be challenging. MoCA on average takes 10–15 min to complete for each dialysis patient and requires trained personnel to administer and score the tests [19]. It is both time-consuming and costly to administer MoCA in all patients especially in settings with staff shortage and limited training resources.

In light of this challenge, short self-reported measures may be a viable alternative that offers the benefits of brevity and ease of administration and interpretation, and may allow for universal cognitive screening in dialysis settings [22]. In a recent systematic review of 221 studies on SCCs in end-stage kidney disease, a total of 13 self-reported measures of SCCs used in this population were identified [3], including questionnaires specifically designed to measure SCCs, composite measures with a cognition subscale, and cognition-related items in electronic item banks. Among these, the Kidney Disease Quality of Life Cognitive Function subscale (KDQOL-CF) [22] was the most frequently used measure; more than 90% of the 221 included studies employed this measure [3]. This tool consists of three items that inquire about patients' experiences with slow reaction time, concentration difficulties, and confusion over the past four weeks. This tool may be particularly well-suited for renal settings globally, as it is available in various languages, is already in use, and does not necessitate extensive training. Patients can self-administer and complete it within one minute, making it a highly feasible alternative to objective cognitive measures. However, only two studies have validated the KDQOL-CF, with inconclusive results.

Kurella et al. assessed the KDQOL-CF in 79 HD patients and 78 non-dialysis patients with stage 3–5 chronic kidney disease [22]. They found a significant correlation between KDQOL-CF scores and performance on the Modified MMSE (3MS). The authors also recommended a cut-off point of 60 (out of 100) on KDQOL-CF to identify objective CIs, with a specificity of 82% and sensitivity of 52% [22]. A limitation of this study,

however, was the use of 3MS as the reference standard, which may underestimate the prevalence of executive functional impairment due to its primary focus on memory. A subsequent validation study was conducted using a more comprehensive neuropsychological battery. In the 168 HD patients recruited, Sorensen et al. found no correlation between KDQOL-CF scores and objective cognitive performance [23]. It was also found that a cut-off point of 60 on KDQOL-CF had generally poor sensitivity (28–36%) and modest specificity (77–81%) in identifying executive functional and memory impairments [23]. It was hence concluded that KDQOL-CF is a poor determinant of objective cognitive performance.

Both validation studies determined the clinical utility of KDQOL-CF solely based on its relevance to neuropsychological tests. However, KDQOL-CF is essentially a measure of SCCs and hence its validity should also be examined against established SCC measures. Moreover, the cognitive domains assessed in the neuropsychological tests of these two studies were not well aligned with the content of KDQOL-CF items. Most notably, both validation studies adopted objective tests of memory ability [22, 23], but memory complaints were not assessed in the KDQOL-CF measure. This lack of memory item is problematic since memory impairments are common in the dialysis population [1], and are often considered an important barrier to treatment adherence [24]. As such, the current study aimed (1) to develop an extended version of KDQOL-CF with the addition of a new memory question, (2) to validate the original and extended versions of KDQOL-CF against established measures of objective and subjective CIs, (3) and to examine associations between the KDQOL-CF and other key endpoints such as functional disability and treatment adherence.

Methods

Participants

A convenience sample of HD patients was recruited from the National Kidney Foundation Singapore (NKF). The inclusion criteria were: (1) 21 years of age or older, (2) diagnosed with end-stage kidney disease and have undergone HD treatment for at least 3 months, and (3) fluent in either English or Mandarin. The exclusion criteria were: (1) only fluent in dialects, (2) unable to give consent due to psychiatric diagnoses or established diagnosis of dementia, or (3) unable to complete survey/assessment due to visual or hearing impairments.

Procedure

The study protocol was approved by the institutional review board of Nanyang Technological University (IRB-2021-025). A list of eligible patients was provided by the nurse managers at each dialysis centre. Study team members fluent in the patients' preferred language approached each patient during one of their regular dialysis sessions. Following written informed consent, the following instruments were administered. Upon completion, patients were given a cash reimbursement.

Measures

Objective cognitive function The Montreal Cognitive Assessment (MoCA) was used as the reference standard for objective CIs in the current study. The MoCA is a brief cognitive screening test that assesses visuospatial and executive functions (i.e., Trail-Making Test part B, cube copy, clock drawing, abstraction), attention (i.e., digit span forward and backward, vigilance, serial-7 subtraction), short-term memory (i.e., delayed recall), language (i.e., naming, sentence repetition, verbal fluency), and orientation (i.e., awareness of time and place) [25]. The test was administered by trained interviewers. The total score of MoCA can range from 0 to 30. A cut-off score of 23.5 has been suggested as the optimal threshold (99% sensitivity and 74% specificity) to differentiate HD patients with and without CIs [18].

Subjective cognitive function The Kidney Disease Quality of Life (KDQOL) instrument is a self-administered questionnaire designed to assess health-related quality of life in patients with kidney disease [26, 27] and has been validated in HD patients in Singapore [28, 29]. Its cognitive function subscale (i.e., KDQOL-CF) assesses SCCs using three items: "How much of the time during the past 4 weeks did you (1) react slowly to things that were said or done, (2) have difficulty concentrating or thinking, and (3) become confused" [22]. In the current study, we added a new item to this measure in order to capture memory complaints (i.e., "How much of the time during the past four weeks did you have memory difficulties?"). Participants were asked to respond to each item on a six-point Likert scale, which were then transformed to scores ranging from 0 to 100 (0=all of the time, 20=most of the time, 40=a good bit of the time, 60=some of the time, 80=a little of the time, 100=none of the time) [22]. The total score of KDQOL-CF is the average of all items and can range from 0 to 100, with higher scores indicating better self-perceived cognitive functioning [26, 27].

We also administered the 33-item Patient's Assessment of Own Functioning Inventory (PAOFI) as a gold standard measure for SCCs [30]. This measure assesses the frequency of experienced everyday cognitive difficulties in four domains: memory (10 items; e.g., "How often do you forget people whom you met in the last day or two?"), language (nine items; e.g., "How often do you have difficulty thinking of the names of things?"), motor/sensory-perceptual ability (five items; e.g., "How often do you have difficulty feeling things with your right hand?"), and higher-level cognitive functions (nine items; e.g., "How

often do you have difficulty finding your way about?"). Participants rated on a six-point Likert scale (1=almost never, 2=very infrequently, 3=once in a while, 4=fairly often, 5=very often, 6=almost always) [30]. Higher scores indicate more frequent SCCs. Woods et al. suggested that the presence of three or more items on PAOFI endorsed as "almost always", "very often", or "fairly often" is indicative of the presence of SCCs [31]. This cut-off point has also been used in other patient populations including HIV [31, 32] and cancer patients [33] to diagnose neurocognitive disorders.

Functional impairment We assessed functional impairment using the Work and Social Adjustment Scale (WSAS) [34]. Participants rated their self-perceived functional impairment in five domains (i.e., work, home management, social leisure activities, private leisure activities, and social relationships) due to cognitive difficulties on a nine-point Likert scale ranging from 0 (i.e., "not at all impaired") to 8 (i.e., "very severely impaired").

Treatment adherence Patients' self-reported medication adherence was measured by the five-item Medication Adherence Report Scale (MARS-5 ©Professor Rob Horne), which was rated on a five-point scale ranging from "never" to "always" [35]. A higher total score indicates poorer medication adherence. The Dialysis Diet and Fluid non-adherence Questionnaire (DDFQ) was also assessed, which is a four-item scale that assesses frequency and degree of dietary and fluid nonadherence in dialysis patients [36]. No total score can be calculated for DDFQ. Instead, four scores were derived, each representing a distinct aspect of adherence (i.e., frequency of diet nonadherence, degree of diet nonadherence, frequency of fluid nonadherence, and degree of diet nonadherence).

Sociodemographic and clinical information Self-reported demographic information was collected, including age, gender, ethnicity, education, relationship status, and employment status. Clinical information including primary kidney disease diagnosis, comorbidities, duration on HD, dialysis adequacy (Kt/V), and medication count, were extracted from patients' medical record.

Statistical analyses

Statistical analyses were performed in R 4.2.2 [37]. Descriptive statistics were computed for sociodemographic, clinical, and cognitive variables. To validate the extended KDQOL-CF, we first conducted a confirmatory factor analysis (CFA) to determine the dimensionality of this four-item scale. Model fit was assessed based on the Comparative Fit Index (CFI), Tucker–Lewis Index (TLI), the Root Mean Square Error of Approximation (RMSEA), the Standardised Root Mean Square (SRMR), and the Chi-square [38]. Good model fit was indicated by CFI and TLI values above 0.95, RMSEA values lower than 0.06, and SRMR values lower than 0.08 [38, 39]. Internal consistency of the extended KDQOL-CF was then examined using Cronbach's alpha, alpha if item deleted, corrected item-scale correlations, and inter-item correlations [40]. Internal consistency was considered acceptable if (1) Cronbach's alpha was greater than 0.70, (2) deleting any item decreased the alpha, (3) corrected item-scale correlations were greater than 0.50, (4) inter-item correlations ranged from 0.15 to 0.85, and (5) average inter-item correlation was between 0.15 and 0.50 [40]. We also assessed the convergent validity (i.e., the degree to which two measures that theoretically should be related, are in fact related) of the extended KDQOL-CF by performing correlation analyses between KDQOL-CF scores and scores on MoCA and PAOFI. Receiver operating characteristic (ROC) curve analysis was conducted to determine the diagnostic ability of the original and extended versions of KDQOL-CF in identifying patients with objective CIs based on MoCA and patients with SCCs based on PAOFI. The area under curve (AUC) was used as a global measure of diagnostic accuracy. An AUC lower than 0.6 was considered bad or not useful, whereas an AUC between 0.6 and 0.7 was considered sufficient, and an AUC above 0.7 was considered good [41]. Finally, we examined differences in functional impairment and treatment adherence between patients scoring below vs. above the optimal cut-off points on the original and extended KDQOL-CF.

Results

Participant characteristics

A total of 369 eligible HD patients in NKF dialysis centres were invited to the study from May to November 2022. Two-hundred-and-sixty-eight patients agreed to participate (response rate 72.6%). The main reasons for rejection were lack of interest and feeling unwell. Table 1 reports the sociodemographic and clinical profiles of the sample, as well as scores on cognitive measures. The mean age of the sample was 59.87 (SD=11.72). The majority of patients were male (57.5%), Chinese (56.3%), and with secondary education (50.6%). Patients on average had been on HD for 78.85 months (SD=62.80). All patient participants at the time of study were on a high-flux HD regimen that comprised three four-hour sessions per week.

Confirmatory factor analysis

We performed a CFA to test whether the four items of KDQOL-CF can be explained by one general factor. Results showed that the one-factor model had excellent fit: CFI=0.999, TLI=0.998, RMSEA=0.021,

Table 1 Sample characteristics (*N* = 268)

	Mean (SD) / *N* (%)
Sociodemographic	
Gender	
Male	154 (57.5%)
Female	114 (42.5%)
Age (years)	59.87 (11.72)
Ethnicity	
Chinese	151 (56.3%)
Malay	80 (29.9%)
Indian or others	37 (13.8%)
Highest education	
Primary or lower	65 (24.9%)
Secondary	132 (50.6%)
Post-secondary or higher	64 (24.5%)
Relationship status	
In a relationship	182 (67.9%)
Not in a relationship	86 (32.1%)
Work status	
Working	76 (28.5%)
Not working	191 (71.5%)
Clinical	
Primary diagnosis	
Diabetic nephropathy	122 (45.5%)
Glomerulonephritis	49 (18.3%)
Hypertension	36 (13.4%)
IgA nephropathy	12 (4.5%)
Others/uncertain aetiology	49 (18.3%)
Presence of diabetes	145 (54.3%)
Presence of hypertension	232 (86.9%)
Presence of hyperlipidaemia	143 (53.6%)
Presence of cardiovascular disease	141 (52.8%)
Duration on HD (months)	78.85 (62.80)
Medication count	12.76 (4.25)
Dialysis adequacy (Kt/V)	1.60 (0.24)
Cognitive	
MoCA	21.49 (4.29) Range: 9–30
PAOFI	1.99 (0.70) Range: 1.00-5.39
Original KDQOL-CF	82.54 (17.81) Range: 0-100
Extended KDQOL-CF	81.90 (16.72) Range: 5-100

Notes. N = Sample size. SD = Standard Deviation. HD = Haemodialysis. MoCA = Montreal Cognitive Assessment. PAOFI = Patient's Assessment of Own Functioning Inventory. KDQOL-CF = Kidney Disease Quality of Life Cognitive Function subscale

SRMR = 0.015, $\chi^2(2) = 2.237$ ($p = .327$). This confirmed the unidimensionality of the 4-item KDQOL-CF.

Internal consistency

Table 2 reports data on the internal consistency of the extended KDQOL-CF. The Cronbach's alpha was 0.80. Cronbach's alpha if item deleted ranged from 0.69 to 0.78, suggesting that removing any item from the scale would decrease the overall alpha. Corrected item-scale correlations were all greater 0.50. Inter-item correlations ranged from 0.40 to 0.61, and the average inter-item correlation was 0.50, which were all within the recommended ranges. These results showed that the extended KDQOL-CF has good internal consistency.

Convergent validity

We then examined correlations between KDQOL-CF items and scores on MoCA and PAOFI to establish the convergent validity of the extended KDQOL-CF (see Table 3). The three original KDQOL-CF items each correlated significantly with performance on visuospatial/executive, attention, and language subtests of MoCA, but were not associated with performance on memory or orientation subtests. The new memory item was significantly correlated with performance on attention, memory, and language subtests of MoCA. This memory item was the only item in the extended KDQOL-CF that correlated with the MoCA memory score. The KDQOL-CF scores were also correlated with PAOFI scores, with moderate effect sizes. The new memory item had the strongest correlation with the PAOFI memory subscale among other KDQOL-CF items.

ROC curve analysis

ROC curve analyses were performed to examine the diagnostic ability of the original and extended versions of KDQOL-CF in identifying objective CIs (see Fig. 1). When using the MoCA cut-off point as the reference standard for objective CIs, the AUC for the original and extended versions of KDQOL-CF were 62.3% and 60.9%, respectively, which were both considered sufficient. There was no significant difference between these two ROC curves ($p = .183$). A cut-off point of 85 on the extended KDQOL-CF achieved the greatest balance between sensitivity and specificity (specificity = 57.9%,

Table 2 Internal consistency of the extended kidney disease quality of life cognitive function subscale

KDQOL-CF items	Cronbach's alpha if item deleted	Corrected item-scale correlations	Inter-item correlations			
			1	2	3	4
1. Slow reaction time	0.75	0.61	-			
2. Concentration difficulty	0.69	0.72	0.60	-		
3. Confusion	0.75	0.59	0.45	0.61	-	
4. Memory difficulty	0.78	0.53	0.44	0.49	0.40	-

Notes. All correlations reported in this table were statistically significant. KDQOL-CF = Kidney Disease Quality of Life Cognitive Function subscale

Table 3 Convergent validity of the extended kidney disease quality of life cognitive function subscale

	Extended KDQOL-CF				
	Total score	**Slow reaction time**	**Concentration difficulty**	**Confusion**	**Memory difficulty**
MoCA Total	0.24*	0.24*	0.18*	0.16*	0.17*
Visuospatial/Executive	0.18*	0.17*	0.17*	0.16*	0.06
Attention	0.24*	0.23*	0.18*	0.16*	0.18*
Memory	0.12	0.11	0.08	0.04	0.14*
Language	0.20*	0.20*	0.13*	0.15*	0.13*
Orientation	0.01	0.05	-0.02	-0.02	0.03
PAOFI Total	-0.72*	-0.54*	-0.59*	-0.57*	-0.59*
Memory	-0.54*	-0.43*	-0.39*	-0.35*	-0.51*
Language	-0.67*	-0.51*	-0.56*	-0.54*	-0.54*
Motor/Sensory-Perceptual	-0.52*	-0.41*	-0.43*	-0.41*	-0.40*
Higher-Level Cognitive	-0.71*	-0.48*	-0.62*	-0.63*	-0.54*

* $p<.050$

Notes. KDQOL-CF=Kidney Disease Quality of Life Cognitive Function subscale. MoCA=Montreal Cognitive Assessment. PAOFI=Patient's Assessment of Own Functioning Inventory

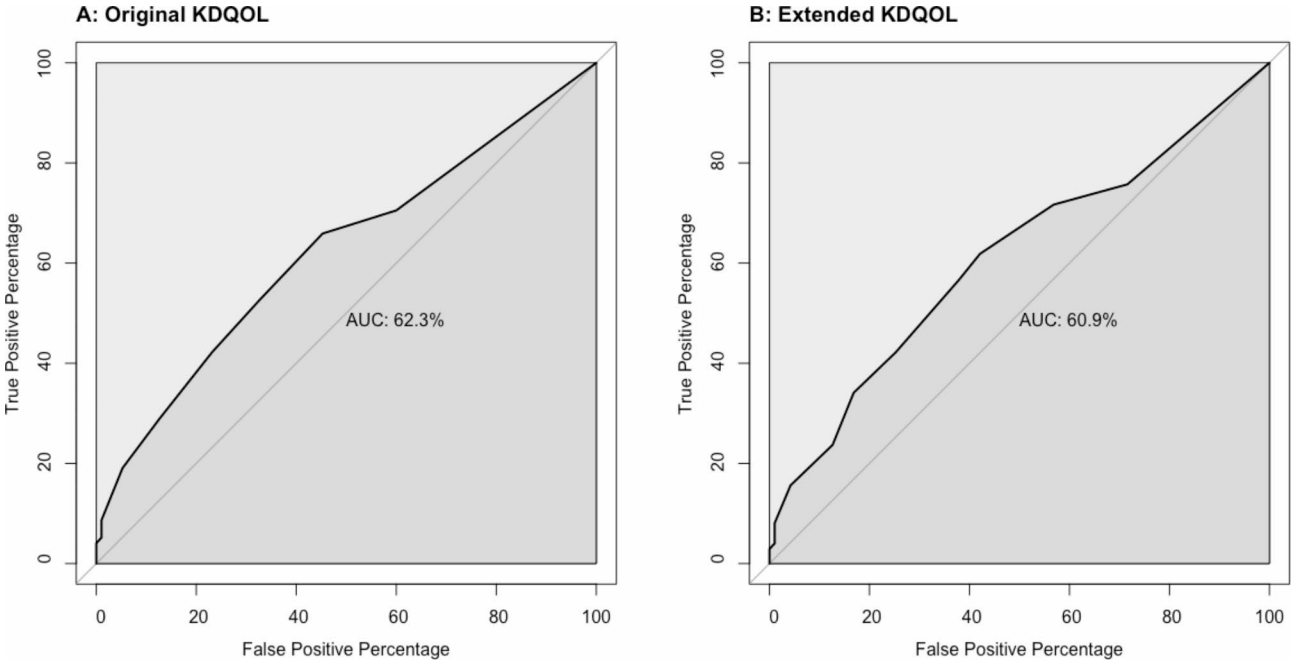

Fig. 1 Receiver operating characteristics (ROC) curve for the original and extended versions of Kidney Disease Quality of Life Cognitive Function subscale (Montreal Cognitive Assessment as the reference standard for objective cognitive impairments)

sensitivity=61.8%, positive predictive value=72.8%, negative predictive value=45.5%). That is, patients who score 85 or lower on the extended KDQOL-CF are considered as having objective CIs.

When using the PAOFI cut-off point as the reference standard for presence of SCCs, the AUC for the original and extended versions of KDQOL-CF were 74.8% and 76.2%, respectively, which were both considered good (see Fig. 2). There was no difference between these two ROC curves ($p=.173$). A cut-off point of 75 achieved the greatest balance between sensitivity and specificity (specificity=78.9%, sensitivity=62.9%, positive predictive value=62.9%, negative predictive value=78.9%). Raising this cut-off point to 85 increased sensitivity to 78.4% but decreased specificity to 58.5%.

Of note, the original cut-off point of 60 on the three-item KDQOL-CF derived by Kurella et al. [22] had very low sensitivity in identifying objective CIs based on MoCA (8.7%), and SCCs based on PAOFI (15.5%), in the current sample.

Associations with other outcomes

- Finally, we compared the original and extended versions of KDQOL-CF in terms of their ability to predict other important dialysis outcomes including

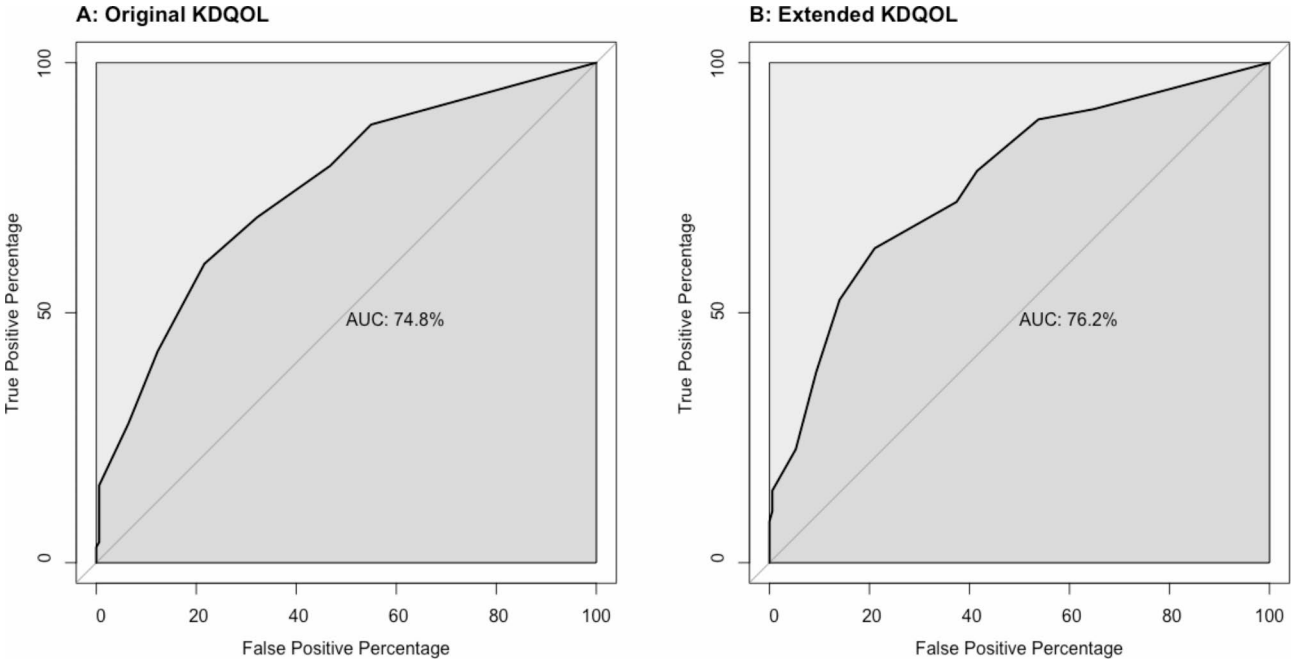

Fig. 2 Receiver operating characteristics (ROC) curve for the original and extended versions of Kidney Disease Quality of Life Cognitive Function subscale (Patient Assessment of Own Functioning Inventory as the reference standard for subjective cognitive complaints)

Table 4 Difference in daily functioning and treatment adherence between patients with and without significant cognitive complaints

	Based on original KDQOL-CF		t-test		Based on extended KDQOL-CF		t-test	
	SCCs (*N* = 16)	No SCC (*N* = 252)			SCCs (*N* = 147)	No SCC (*N* = 121)		
	Means (*SD*)		*p* value	Cohen's *d*	Means (*SD*)		*p* value	Cohen's *d*
WSAS	15.50 (10.92)	5.56 (7.94)	0.002**	1.22	9.62 (9.40)	1.95 (4.37)	< 0.001***	1.02
MARS-5	8.94 (2.93)	7.19 (2.76)	0.015*	0.63	7.90 (3.10)	6.55 (2.17)	< 0.001***	0.50
DDFQ-1	3.47 (5.01)	2.60 (3.86)	0.408	0.22	3.15 (4.19)	2.08 (3.55)	0.030*	0.27
DDFQ-2	1.00 (1.03)	0.99 (0.93)	0.973	0.01	1.10 (0.88)	0.87 (0.97)	0.045*	0.25
DDFQ-3	4.94 (5.07)	2.51 (3.88)	0.078	0.62	3.44 (4.50)	1.75 (3.09)	< 0.001***	0.43
DDFQ-4	1.31 (1.14)	1.01 (0.94)	0.316	0.32	1.20 (0.94)	0.82 (0.92)	< 0.001***	0.42

* $p < .050$. ** $p < .010$. *** $p < .001$.

Notes. KDQOL-CF = Kidney Disease Quality of Life Cognitive Function subscale. SCC = Subjective Cognitive Complaint. N = Group size. SD = Standard Deviation. WSAS = Work and Social Adjustment Scale. MARS = Medication Adherence Report Scale. DDFQ = Dialysis Diet and Fluid non-adherence Questionnaire. DDFQ-1 = number of days in the past two weeks during which patients did not follow diet guidelines. DDFQ-2 = the extent to which patients deviated from diet guidelines. DDFQ-3 = number of days in the past two weeks during which patients did not follow fluid guidelines. DDFQ-4 = the extent to which patients deviated from fluid guidelines

functional impairment and treatment adherence (see Table 4). We classified study participants into two groups based on the cut-off point of 60 on the original KDQOL-CF (i.e., a score < 60 considered as having SCCs) and compared their scores on WSAS, MARS-5, and DDFQ. Patients with SCCs based on the original KDQOL-CF had more severe functional impairment and medication nonadherence compared to those without, but there was no difference in dietary and fluid adherence. We then classified patients into two groups based on the newly-derived cut-off point of 85 on the extended KDQOL-CF. Patients with SCCs based on the extended KDQOL-CF had more severe functional impairment, and medication, fluid, and diet nonadherence, compared to those without.

Discussion

The high prevalence rate of CIs in HD patients, coupled with logistical constraints that hinder the implementation of neuropsychological assessments in routine care, highlight the need for self-reported cognitive screeners, but the validity and suitability of existing self-report tools have been called into doubt. In this study, we validated an extended version of the KDQOL-CF with the addition of a memory item. Our findings indicate that the extended KDQOL-CF exhibit unidimensionality, good internal

consistency, and convergent validity as evidenced by significant correlations with established measures of objective and subjective CIs. The derived cut-off point of 85 (out of 100) on the extended KDQOL-CF offers a practical threshold for identifying HD patients with objective CIs and/or SCCs, demonstrating superior performance compared to the original version in predicting functional impairment and treatment nonadherence.

One key finding was the significant associations between the extended KDQOL-CF and performance on MoCA. Most notably, the new memory item was the only item within KDQOL-CF that correlated with performance on the delayed recall task which assesses short-term memory. The memory item was also correlated with performance on attention and language subtests of MoCA. It could be that some of these subtests such as backward digit span and sentence repetition required participants' working memory, hence were associated with subjective memory complaints. These findings suggest that the inclusion of the memory item in the KDQOL-CF is essential to improve the scale's ability to capture memory impairments and complaints. Previous research has shown that HD patients perform significantly worse on memory tasks compared to non-dialysis patients and the general population [24, 42, 43]. Self-reported forgetfulness and impairments in both retrospective and prospective memory are also key barriers to treatment adherence in the context of dialysis [24, 44, 45]. The omission of memory domain in the original KDQOL-CF is therefore problematic.

Despite the significant associations between the extended KDQOL-CF and MoCA scores, it is of note that these correlations were generally weak in magnitude. Also, ROC curve analysis showed modest sensitivity (61.8%) and specificity (57.9%) of the extended KDQOL-CF in classifying MoCA status. The implication is that a score higher than 85 on the extended KDQOL-CF may not necessarily indicate intact cognition. Indeed, research in the Alzheimer's disease literature suggests that individuals with more advanced CIs may have diminished insight, a phenomenon known as anosognosia, where individuals are unable to recognise their own cognitive deficits [46]. This suggests that the predictive power of subjective cognitive measures such as KDQOL-CF may be stronger at earlier stages of kidney disease and the preclinical stage of CIs, where individuals start experiencing subtle cognitive changes in everyday life while exhibiting normal performance on objective tests [17]. This highlights the potential of KDQOL-CF to be administered periodically in renal settings to monitor patients' cognition prior to the diagnosis of kidney failure or initiation of dialysis before CIs become too severe or irreversible. Nevertheless, the sensitivity of the extended KDQOL-CF reported in the current study is already higher than that of the original cut-off point on the three-item KDQOL-CF (i.e., 52% in Kurella et al. [22]; 28–36% in Sorensen et al. [23]; 8.7% in the current study). It could be that the additional memory item improved the measure's ability in detecting memory impairments. Future studies need to determine an optimal set of SCC items that captures complaints in various domains to achieve better diagnostic accuracy.

The current study is the first attempt to validate the KDQOL-CF against a comprehensive SCC questionnaire. There is a growing recognition that SCCs comprise a valid clinical endpoint and a core patient-reported outcome even in the absence of objective CIs. These complaints may represent a preclinical stage of cognitive decline that predicts future progression [17], and may indicate an increased risk of impairments in decision-making, self-care, and functional capacity [4, 5, 9]. In the current sample, patient responses to the extended KDQOL-CF and PAOFI were moderately correlated. These correlations also showed domain specificity where the new memory item, among all four KDQOL-CF items, had the strongest correlation with the memory subscale of PAOFI. The utility of the extended KDQOL-CF to identify SCCs in HD patients was further supported by ROC curve analysis where a score of 75 was considered the optimal cut-off. However, as a first-stage screening tool in prevalent HD patients where sensitivity should be preferred, we recommend adopting a cut-off point of 85 (same as the cut-off for identifying objective CIs) which has a sensitivity of 78.4% and specificity of 58.5%. This cut-off point was also able to identify patients at risk of functional impairment and treatment nonadherence, which may allow for early intervention and initiation of support strategies in clinical practice.

Overall, the current study suggests a need to include a memory item in the KDQOL-CF measure and a need to raise its cut-off point on the extended scale. When dialysis patients report SCCs on the extended KDQOL-CF, it may simultaneously indicate the presence of objective CIs that need further neuropsychological evaluation, the presence of everyday cognitive difficulties that need to be supported or compensated with cognitive rehabilitative interventions, and potential functional disability and treatment nonadherence that need to be addressed to improve prognostic outcomes. Although there is still room for improvement regarding the predictive power of KDQOL-CF, it should be highlighted that its current classification accuracy was achieved using only four self-reported items that can be completed by patients within one minute without the need for trained staff. Self-reported cognitive screeners such as the extended KDQOL-CF may prove to be a cost-effective first-stage screener in a step-up diagnostic framework, followed by

more comprehensive cognitive assessments (e.g., MoCA), referral to specialists, and revision of the care plan.

Currently, however, there is a lack of established protocol in renal settings to address HD patients' cognitive challenges following identification. Interventions aimed at improving toxin clearance through novel dialysis modalities, such as nocturnal daily HD [14] and haemodiafiltration [15], have demonstrated cognitive advantages over conventional HD. Lifestyle interventions such as intradialytic cycling and cognitive training through tablet games have also shown potential to enhance cognitive function among HD patients [10]. Besides facilitating interventions that directly target cognition, it is of note that the identification of cognitive difficulties through tools like the extended KDQOL-CF serves a broader purpose. The results of cognitive screening can be used as a reference for healthcare providers to adjust their approach to patient care. For instance, providers may tailor communication strategies to patients' cognitive capacity, using simpler instructions and clearer language. Involving family members in the care process is particularly important to ensure the safety and well-being of patients with cognitive issues. Furthermore, given the increased risk of nonadherence in patients with SCCs as evidenced in this study, it may be necessary to consider strategies to modify and/or support the complex medical regimen prescribed to this subgroup. In this light, cognitive screening in renal settings is not merely a precursor to intervention but also a cornerstone for delivering patient-centred care.

Research on the clinical utility of SCC measures is still in its infancy. In dementia research, SCCs are considered a prodromal marker of CIs [17]. In the context of cancer, SCCs serve as a stand-alone outcome measure that has important patient implications [47]. In kidney disease research, however, SCCs have frequently been assessed as a secondary outcome, and in some studies regarded as a mere reflection of psychological distress. While neuropsychological tests remain the gold standard measure of cognition, they are not the sole indicators of overall cognitive well-being. We therefore propose three future directions in this area. First, there is growing evidence in the Alzheimer's disease literature showing that SCCs emerge prior to clinical CIs and constitute an independent risk factor for progression to dementia [17, 48–50]. However, the role of SCCs as a prodromal marker in the context of kidney disease remains to be tested. Relatedly, self-reported measures such as the KDQOL-CF may be a more sensitive tool in earlier stages of chronic kidney disease when CIs are milder than in advanced stages post-dialysis initiation. These hypotheses should be investigated in future longitudinal studies. Another important next step would be to relate subjective cognitive measures to more comprehensive assessments of neuropsychological, neuroimaging, and biological parameters of CIs to further confirm their convergent validity. Third, to overcome the limitations of self-report in stages of severe CIs where anosognosia may be present, informant-report of SCCs may be particularly useful. Research has indicated that informant-reports are more accurate than self-reports at advanced stages of dementia [17], and are an independent predictor of diagnostic conversion to objective CIs [51]. Exploring caregivers' perspective of patients' cognitive abilities may be a fruitful area of future research.

While this study focuses on validating the extended KDQOL-CF, a conventional pencil-and-paper questionnaire, computerised methodologies such as the Patient Reported Outcome Measurement Information System (PROMIS), developed based on item response theory to calibrate items, may also be a viable alternative for routine testing as these enable computerised adaptive testing and a time-efficient and personalised assessment [52]. The application of PROMIS for evaluating SCCs in kidney disease research has only emerged recently [15, 53]. While we recognise that these features offer great advantages for use in dialysis settings, our decision to concentrate on the KDQOL-CF was driven by its widespread acceptance and utilisation in research, clinical trials, and clinical practice globally [3]. By adding a memory item to KDQOL-CF, we provide clinicians with an easily administered tool to screen for cognitive difficulties before assessor-administered evaluation such as MoCA are recommended.

Some limitations warrant acknowledgement. The extended KDQOL-CF was validated in a sample of prevalent HD patients who had been on dialysis for an average of six years at the time of assessment. More work is needed to evaluate the utility of this measure in other kidney disease segments such as incident HD patients, and patients on other treatment modalities such as peritoneal dialysis. This will enable careful calibration of cut-off points for different subgroups and identification of the most suitable self-report screener to support timely diagnosis and care across the spectrum of this population. To this end it is also important to note that the sample comprised individuals of Asian ancestry, hence generalisability of findings to other ethnic groups could not be ascertained. The other two validation studies of KDQOL-CF were both conducted in the US, comprising mainly Caucasian participants [22, 23]. It is possible that the optimal cut-off points differed as a function of ethnic background of the recruited sample due to different cultural values towards dementia that may impact willingness for self-disclosure and help seeking [54].

Conclusions

In summary, this study reports the psychometric properties of an extended version of the KDQOL-CF measure that includes a new memory item. Our findings suggest that the extended KDQOL-CF is a valid and reliable questionnaire for identifying objective and subjective CIs among prevalent HD patients in Singapore. The extended KDQOL-CF also identifies HD patients at risk of functional impairment and treatment nonadherence. The KDQOL-CF is currently the most frequently used SCC measure in renal settings [3]. To improve its clinical utility, we recommend researchers and healthcare providers interested in this measure to include the additional memory question and consider adopting the new cut-off point to aid interpretation of patient responses. We need more research to determine an optimal set of SCC items that are brief and accurate so that they could be used in renal settings to maximise efficiency of cognitive screening.

Abbreviations

AUC	Area under curve
Cis	Cognitive impairments
CFI	Comparative Fit Index
CFA	Confirmatory factor analysis
DDFQ	Dialysis Diet and Fluid non-adherence Questionnaire
HD	Haemodialysis
KDQOL-CF	Kidney Disease Quality of Life Cognitive Function subscale
MARS-5	Medication Adherence Report Scale
MMSE	Mini-Mental State Examination
3MS	Modified MMSE
MoCA	Montreal Cognitive Assessment
NKF	National Kidney Foundation Singapore
PAOFI	Patient's Assessment of Own Functioning Inventory
ROC	Receiver operating characteristic
RMSEA	Root Mean Square Error of Approximation
SD	Standard deviation
SRMR	Standardised Root Mean Square
SCCs	Subjective cognitive complaints
TLI	Tucker–Lewis Index
WSAS	Work and Social Adjustment Scale

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Author contributions

FC, PS, and PL recruited patients and collected data. BK and JC provided clinical data of consented patients. FC and KG analysed and interpreted the data. FC wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the institutional review board of Nanyang Technological University and are in compliance with the Helsinki declaration. Informed consent of each participant was obtained before the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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