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The Burden of Cognitive Impairment in Patients With End-Stage Renal Disease and Impact on Dialysis Modality Choice

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Introduction: Kidney disease is associated with significant cognitive dysfunction. Subjective reports of cognitive ability have not been studied extensively in chronic kidney disease. We investigated the association between objective and subjective cognitive functions in predialysis patients and their association with self-care dialysis modality choice.

Methods: Cross-sectional data from the Barriers to Successful Implementation of Care in Home Haemodialysis study were used for the study of cognition in 220 predialysis patients. The data were used to ascertain the demographics, clinical, laboratory, and neuropsychometric variables. The latter includes Trail Making Tests (TMT) parts A and B, Modified Mini Mental State Examination, and metacognition questionnaire for subjective assessment of one's cognitive ability. The outcome variable was fully assisted and self-care dialysis modality choice.

Results: Within the study cohort, 90 patients chose fully assisted hemodialysis and 114 patients chose self-care dialysis. The median Modified Mini Mental State Examination, TMT part A, and TMT part B scores were greater for the assisted versus the self-care group. Metamemory was not significantly different between groups, but the metaconcentration score was significantly worse in the group choosing assisted dialysis. Higher (i.e., better) metaconcentration scores were significantly associated with the self-care modality choice in the univariate and hierarchical regression analyses. Adjusted and unadjusted analyses showed a significant association between perceived concentration and TMT part B scores ($P < 0.01$). With every 1.6-minute increase in TMT part B score, there was a 1-unit reduction in metaconcentration score, and the latter was associated with 20% lower odds of choosing self-care dialysis over a fully assisted dialysis modality.

Discussion: Patients' self-perception of cognitive ability is a significant predictor of self-care dialysis modality choice. Subjective report of "metaconcentration" is also strongly associated with poorer outcome on the TMT part B.

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Chronic kidney disease (CKD) is a worldwide public health issue.[1,2] Cognitive deficits in CKD patients are increasingly being recognized as a major problem, with a 3-fold increase in this group compared to that in the general population.[3] The management of cognitive deficits very early in the course of CKD is desirable, as more advanced stages of kidney disease are associated with greater impairment of cognitive function.[4] In 1 study, participants with mild, moderate, and severe renal impairment were compared, and the authors concluded that for every 10-ml/min decrease in estimated glomerular filtration rate, the risk of cognitive dysfunction increased by 15% to 25%.[5] This issue is more of a problem in older individuals and in those established on dialysis, with a prevalence of cognitive impairment in hemodialysis patients estimated to be about 30% to 70%.[6] The presence of cognitive impairment in this cohort is also associated with higher mortality.[7,8] The pathogenesis of the accelerated cognitive decline in CKD is attributable to vascular injury from traditional risk factors, and from direct neuronal toxicity of uremic retention solutes.[9] It is believed that microvascular disease of the brain is responsible for the pattern of cognitive deficits seen in kidney disease and that it is related to the patients' vascular risk profiles. This is typically manifest as impaired executive brain function.

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The focus on cognition in CKD is extremely important, as the notion of self-care dialysis relies on cognitive intactness. Patient participation, patient choice, and patient-led decision making are associated with better outcomes and are therefore considered best clinical practice.[10–12] There is greater impetus for self-management of long-term conditions,[13,14] but the cognitive context in which such decisions are made by patients is not well understood and merits further research. This applies to both objective cognitive deficits and patients' assessment of their own cognitive ability (subjective cognitive ability). The latter is grossly underrepresented in kidney disease literature.

Few studies have been published to date, in regard to patients with kidney disease, that specifically seek to examine the association between subjective and objective cognition assessments.[15,16] The Kidney Disease Quality of Life (KDQOL)—Cognitive Function subscale with 3 questions was shown to be a limited instrument for accurately assessing subjective cognitive function[16] and bore no relationship to the executive function test, which is commonly abnormal in chronic kidney disease.[17–19] More recently, a study found modest correlation between subjective and objective assessments; however, the former was a predictor of the patient's self-reported measure of activities of daily living, although both subjective reports may well be influenced by negative affectivity.[15,20] In other population groups, subjective assessment of impaired cognition has been associated with poorer health-related quality-of-life, reduced daily functioning,[21] and increased risk of hospital attendance,[22,23] and is also predictive of future cognitive decline.[24–26] In addition, the identification of cognitive impairment is important in order to assist patients in making well-informed treatment decisions, in ensuring treatment compliance, and in helping to prevent functional decline.[27] Treatment decision making is multifactorial and includes, among other factors, the patient's and health care professional's perception (whether accurate or not) of the patient's cognitive abilities. The choice of self-care dialysis decisions is expected of patients after information on dialysis modalities is provided to them. Hence, the possibility of the influence of the patients' assessment of how their memory works, and how they judge their own abilities and effectiveness, may predict their choice of dialysis modality.

The aims of the present study are as follows: (1) to assess metacognition in patients with CKD-5 (predialysis phase of end-stage renal disease) as a measure of subjective cognitive impairment and to explore the association between subjective and objective cognition tests; and (2) to examine associations of dialysis modality choice (fully assisted vs. self-care) with measures of objective (global cognition and executive brain function) and subjective cognition assessments (memory and concentration).

MATERIALS AND METHODS

Participants and Recruitment

Data for the present study are derived from that ascertained for the Barriers to Successful Implementation of Care in Home Haemodialysis (BASIC-HHD) study.[28] The data were prospectively collected for a comprehensive and systematic study of barriers to and enablers of the uptake of self-care dialysis therapy. The study involves 5 centers in the United Kingdom, with variable prevalence rates of home hemodialysis (HD). An integrated mixed methodology (convergent, parallel design) has been adopted for the BASIC-HHD study in a combined cross-sectional and prospective study design. The methodological details and scope of data collected in the BASIC-HHD appear in a published protocol.[28] Data presented here are derived from the CKD-5, a predialysis cohort of the BASIC-HHD study. A total of 222 patients were enrolled in this group. Predialysis patients were approached if they fulfilled eligibility criteria and were willing to undertake neuropsychometric assessments and to complete study specific questionnaires.

Study Registration

This study was reviewed and approved by the Greater Manchester West Health Research Authority National Research Ethics Service (NRES) (Reference number: 12/NW/0170). The study is on the NIHR portfolio (ID 12346). Written informed consent from participants was obtained for the study. Psychological measures used in this study were part of a compilation of questionnaires. Blood sampling and neuropsychometric assessments were carried out at patients' routine hospital clinic visits. Visually impaired participants were excluded from this analysis (n = 2).

Independent Variables

Independent variables included the following: objective tests of cognition, Trail Making Tests (TMT) parts A and B,[29] Modified Mini Mental State Examination (3MS),[30] subjective assessment of cognition scales (metacognition questionnaire,[31] demographics (age, sex, ethnicity, education, employment, and marital status); clinical variables (Charlson Comorbidity Index [CCI],[32] cause of end-stage renal disease [ESRD], diabetes, heart failure, intracranial vascular events, ischemic heart disease, systolic and diastolic blood pressures); laboratory variables (urea, creatinine, phosphate, parathyroid hormone, bicarbonate, albumin, hemoglobin, and medications including angiotensin-converting enzyme inhibitors, central nervous system—influencing drugs, antidepressants, antiplatelet agents, cholesterol-lowering drugs,

erythropoietin, folic acid, and number of antihypertensive drugs and total pill burden); and psychological screening tools (Beck Depression Inventory [BDI],[33] and State and Trait Anxiety Inventory (STAI).[34]

Cognitive Assessments

Objective Tests

Tests of cognitive function were assessed by study coordinators across all participating centers after completion of training in the application and procedure for using these tests. Only participants conversant in English language were included in this aspect of the study. The 3MS is a test of global cognitive function that includes assessment of orientation, attention, calculation, language, and short-term memory. The Trail Making Tests are a measure of cognitive abilities such as speed and fluid intelligence; they have been hypothesized to reflect a wide variety of cognitive processes including attention, visual search and scanning, sequencing and set shifting, psychomotor speed, abstraction, flexibility, and ability to execute and modify a plan of action. A 3MS score of <80 is deemed deficient. The timed Trail Making Tests parts A and B are deemed insufficient if the duration exceeds 1 SD from the mean of the present study cohort (>87 seconds in part A and >197 seconds in part B). All 3 variables were treated as continuous variables for the purpose of the univariate and multivariable analysis.

Subjective Tests

To enable understanding of the patients' beliefs about their own memory and concentration, the brief metacognition questionnaire was used. This questionnaire has 2 subscales: the metamemory subscale (5 questions) and the metaconcentration subscale (4 questions). Metacognition is highly relevant for sustained independence in older age. This tool has not been validated in the kidney disease population, but the parameters used to assess the outcome, namely independence, was deemed common to both population groups. The responses were given on a Likert scale (1 = strongly disagree, 2 = disagree, 3 = neither agree nor disagree, 4 = agree and 5 = strongly agree) and then summed for each subscale. The range of scores for the metamemory subscale is 5 to 25 and that of the metaconcentration subscale is 4 to 20. A summary of completeness of data provided by the study participants is provided in Table 1.

The TMT part B test data had missing data points that appeared to be missing at both random and not at random. Where patients failed to complete part of the test, the data are considered "missing not at random." Missing at random data included those items for which participants did not complete any data or for which the administration was deemed incorrect. In 8 cases, the data were imputed to 300 seconds where the administrator explicitly mentioned that the patient "gave up" completing the TMT part B test after persisting for some time (missing not at random data). However, of these 8 imputed cases, only 6 were considered for analysis, for which information on modality choice as the outcome was also available.

Table 1. Completeness of data provided by study participants

Number of eligible participants	220
TMT part A	208 (94.5%)
TMT part B	169 (76.8%)
3MS	206 (93.6%)
Metamemory subscale	215 (97.7%)
Metaconcentration subscale	213 (96.8%)
Decision on modality choice (outcome variable)	204 (92.7%)

Statistical Analyses

Analyses were performed using SPSS 22 and STATA 13. A 2-sided 5% significance level was used throughout the analysis. Baseline characteristics were assessed among the 3 modality choices in the predialysis cohort using χ^2 tests, Fisher exact tests, analyses of variance, and Kruskal–Wallis tests, as appropriate.

Single variable analyses using χ^2 tests, Fisher exact tests, independent t tests, and Mann–Whitney U tests, as appropriate, with modality choice as the outcome, grouped as self-care (peritoneal dialysis [PD] and home dialysis) and hospital, revealed which cognitive, medical, and demographic variables were significant. A hierarchical logistic regression analysis was then carried out for each of the cognitive variables (5 models) with modality choice as the outcome. The differences within the self-care group were investigated to assess the suitability of grouping PD and home HD. The relationships between the subjective and objective cognition variables were investigated using correlations and linear regression.

Sensitivity analyses were carried out involving multiple imputation with chained equations to account for missing data in all of the cognition variables based on variables including CCI, age, sex, ethnicity, education, employment, BDI, scores on other tests of objective cognition, and the outcome variable, namely, modality choice (Appendix S1).

RESULTS

Patient Characteristics

There were 220 participants in all. A total of 90 patients chose hospital hemodialysis and 114 patients chose self-care dialysis (PD and home hemodialysis [HHD]). Of these, 52% (114) of patients expressed their preference

Table 2. Characteristics of study participants

	Facility-based HD (n = 90)	PD (n = 78)	Home HD (n = 36)	*P* value
TMT B, median (IQR)	n = 64 102.0 (78.5–132.3)	n = 63 90.0 (63.0–118.0)	n = 30 94.0 (64.5–122.5)	0.11[a]
TMT A, median (IQR)	n = 83 49.0 (32.0–62.0)	n = 74 41.5 (30.0–60.0)	42.8 (31.2–55.9)	0.086[a]
3MS, median (IQR)	n = 85 93.0 (88.5–97.0)	n = 74 95.0 (91.0–98.0)	n = 34 92.5 (88.0–96.5)	0.066[a]
MCQ1 (metamemory), mean (SD)	n = 89 17.7 (3.8)	n = 76 18.2 (3.3)	n = 35 17.4 (4.5)	0.53[b]
MCQ2 (metaconcentration), mean (SD)	n = 88 13.9 (2.4)	n = 74 15.1 (2.8)	14.6 (2.9)	0.016[b]
Age, mean (SD)	62.6 (12.3)	58.3 (12.9)	53.6 (13.0)	0.001[b]
Sex, female	36 (40.0%)	28 (35.9%)	15 (41.7%)	0.80[c]
Education, post high school	19/87 (21.8%)	20/76 (26.3%)	12/35 (34.3%)	0.36[c]
Employment				
Retired	51 (56.7%)	36 (46.2%)	12 (33.3%)	
Unemployed	19 (21.1%)	13 (16.7%)	7 (19.4%)	0.053[c]
Salaried/self-employed	20 (22.2%)	29 (37.2%)	17 (47.2%)	
Ethnicity, nonwhite	12 (13.3%)	3 (3.8%)	5 (13.9%)	0.079[c]
Marital status				
Married or partner	56 (62.2%)	53 (67.9%)	23 (63.9%)	
Single	20 (22.2%)	13 (16.7%)	7 (19.4%)	0.71[d]
Divorced or separated	6 (6.7%)	3 (3.8%)	4 (11.1%)	
Widowed	8 (8.9%)	9 (11.5%)	2 (5.6%)	
Cause of ESRD				
Systemic	50 (55.6%)	29 (37.2%)	13 (36.1%)	
Renal	17 (18.9%)	24 (30.8%)	13 (36.1%)	0.081[c]
Other/unknown	23 (25.6%)	25 (32.1%)	10 (27.8%)	
CCI, median (IQR)	5.0 (4.0–7.0)	4.0 (3.0–6.0)	4.0 (3.0–5.0)	0.009[a]
Diabetes	32 (35.6%)	22 (28.2%)	10 (27.8%)	0.52[c]
Heart failure	4 (4.4%)	4 (5.1%)	1 (2.8%)	>0.99[d]
Ischemic heart disease	18 (20.0%)	18 (23.1%)	6 (16.7%)	0.72[c]
IVE	9 (10.0%)	5 (6.4%)	2 (5.6%)	0.59[c]
Urea, median (IQR)	n = 89 22.6 (18.6–28.2)	n = 77 23.1 (18.6–29.4)	n = 34 23.1 (19.7–26.0)	0.86[a]
Creatinine, median (IQR)	n = 89 377 (338–459)	n = 77 428 (343–524)	n = 34 429 (383–500)	0.046[a]
Hb < 9	3/89 (3.4%)	2/77 (2.6%)	2/35 (5.7%)	0.77[d]
Alb < 30	4/89 (4.5%)	2/77 (2.6%)	0/35 (0%)	0.65[d]
Bic	n = 84	n = 75	n = 35	
<22	37 (44.0%)	32 (42.7%)	17 (48.6%)	
22–28	43 (51.2%)	39 (52.0%)	17 (48.6%)	0.99[d]
>28	4 (4.8%)	4 (5.3%)	1 (2.9%)	
PTH, median (IQR)	n = 86 23.6 (14.0–35.2)	n = 77 22.2 (12.3–35.1)	n = 35 32.3 (17.5–48.3)	0.051[a]
Phosphate	n = 88	n = 76	n = 35	
<1.1	11 (12.5%)	11 (14.5%)	2 (5.7%)	
1.1–1.7	61 (69.3%)	43 (56.5%)	28 (80.0%)	0.14[c]
>1.7	16 (18.2%)	22 (28.9%)	5 (14.3%)	
SBP, ≤115	4/89 (4.5%)	9/76 (11.8%)	1 (2.8%)	0.10[c]
SBP, mean (SD)	n = 89 143.7 (19.2)	n = 76 137.5 (21.4)	140.1 (17.5)	0.14[b]
DBP, >85	16/89 (18.0%)	15/76 (19.7%)	6 (16.7%)	0.92[c]
DBP, mean (SD)	n = 89 76.3 (11.1)	n = 76 77.1 (11.4)	73.4 (11.9)	0.26[b]
ACEI or ARB	41 (45.6%)	47 (60.3%)	21/34 (61.8%)	0.098[c]
Folic acid	10 (11.1%)	11 (14.1%)	5/34 (14.7%)	0.80[c]
No. of antihypertensive drugs, median (IQR)	3.0 (2.0–4.0)	2.5 (2.0–4.0)	n = 34 3.0 (2.0–4.0)	0.28[a]
EPO	31 (34.4%)	30 (38.5%)	8/35 (22.9%)	0.27[c]
CNS	7 (7.8%)	7 (9.0%)	4/34 (11.8%)	0.79[c]
Antidepressants	18 (20.0%)	10 (12.8%)	3/34 (8.8%)	0.22[c]

(Continued on next page)

Table 2. Characteristics of study participants (Continued)

	Facility-based HD (n = 90)	PD (n = 78)	Home HD (n = 36)	*P* value
Antiplatelet agents	39 (43.3%)	24 (30.8%)	13/34 (38.2%)	0.24[c]
Statins/EZE	53 (58.9%)	41 (52.6%)	24/34 (70.6%)	0.20[c]
Pill burden, mean (SD)	7.5 (2.6)	6.9 (2.5)	n = 34 8.2 (3.4)	0.069[b]
BDI, median (IQR)	n = 82 12.0 (5.8–22.3)	n = 70 7.0 (4.0–12.3)	n = 28 9.0 (6.0–14.5)	0.009[a]
STAI State, median (IQR)	n = 80 39.5 (29.3–47.8)	n = 66 32.0 (26.0–40.0)	n = 28 33.0 (25.3–46.0)	0.026[a]
STAI Trait, median (IQR)	n = 79 41.0 (30.0–47.0)	n = 63 34.0 (29.0–46.0)	n = 28 35.0 (27.0–42.8)	0.093[a]

BDI, Beck Depression Inventory; CCI, Charlson Comorbidity Index; CNS, central nervous system; DBP, diastolic blood pressure; EPO, erythropoeitin; ESRD, end-stage renal disease; EZE, ezetemibe; HD, hemodialysis; IVE, intracranial vascular event; IQR, interquartile range; MCQ, Metacognition Questionnaire; PD, peritoneal dialysis; PTH, parathyroid hormone; SBP, systolic blood pressure; STAI, State and Trait Anxiety Inventory; TMT, Trail Making Test; 3MS, Modified Mini Mental State Examination.
[a]Kruskal–Wallis test.
[b]One-way analysis of variance.
[c]Pearson χ^2 test.
[d]Fisher exact test.

for self-care dialysis, 36 patients preferred HHD, and 78 patients preferred PD. The characteristics of these participants are presented in the Table 2. Among the 3 groups overall, significant differences were observed in regard to age, CCI, BDI score, and STAI-S, which were higher in patients choosing fully assisted dialysis. Metaconcentration scores were lowest in participants choosing hospital HD. Parathyroid hormone was significantly higher in the cohort choosing HHD. Within the self-care group, no significant differences were observed in any dependent variable category, including tests of cognition, between participants who chose PD versus HHD.

Cognition Burden in ESRD

In the study cohort, based on the cut-off for identification of objective cognitive deficit (3MS < 80, TMT parts A and B > 1.5 SD from the mean for the study groups), the numbers and proportions of participants with cognitive deficits in the 3 groups are as shown in Table 3.

Univariate Analysis

In the single-variable analysis of the association of key variables of interest with modality choice (Table 4), variables significantly ($P < 0.05$) associated with self-care dialysis modality (PD+HHD) choice, include lower TMT part B scores, lower TMT part A scores, higher metaconcentration scores, lower age, being in employment, "renal-limited" cause of end-stage renal disease, lower CCI, use of drugs such as angiotensin-converting enzyme inhibitors, higher serum creatinine, lower BDI, and lower STAI-S/T scores.

Hierarchical Regression Analysis of Predictors of Self-Care Modality Choice

In the hierarchical regression analysis (Table 5), significant predictors of self-care dialysis modality choice across all models of cognition tests include white ethnicity, lower BDI scores, and lower CCI, after adjustment for other variables in the model. The test of subjective cognitive ability, the metaconcentration subscale, but not the metamemory subscale, was highly significantly associated with self-care modality choice ($P < 0.01$). TMT parts A and B and 3MS were not statistically significant predictors of modality choice after adjustment for CCI (age is factored into CCI), BDI, employment, ethnicity, and sex, although the direction of effect suggests that better scores on tests of cognition are associated with the choice of self-care dialysis modality.

Association Between Objective and Subjective Cognitive Assessments

In the adjusted analysis (adjusted for CCI, BDI, and education) (Table 6) of the association among TMT parts A and B, 3MS, and the metamemory and metaconcentration subscales, a significant association was noted between TMT part B and the metaconcentration scale ($P < 0.01$). A parameter estimate of −0.10 suggests a small (0.1-unit) change in metaconcentration score with a 10-second increase in TMT part B. Therefore, with every 1.6-minute increase in TMT part B, there is a 1-unit reduction in metaconcentration score, and this is associated with 20% lower odds of choosing a self-care modality over HDD.

DISCUSSION

The cognitive ability assessment of predialysis CKD-5 patients is a window into the patient's ability to ascertain, retain, and process information and to come

Table 3. Participants with cognitive deficits, by dialysis type

	Overall	Hospital	PD	Home HD
3MS (<80)	6/193 (3.1%)	3/85 (3.5%)	1/74 (1.4%)	2/34 (5.9%)
TMT part A (>87)	15/193 (7.8%)	7/83 (8.4%)	6/74 (8.1%)	2/36 (5.6%)
TMT part B (>197)	12/157 (7.6%)	6/64 (9.4%)	3/63 (4.8%)	3/30 (10.0%)

Home HD; home hemodialysis; PD, peritoneal dialysis; TMT, Trail Making Test.

Table 4. Univariate analysis of study variables with modality choice as outcome

	Facility-based HD (n = 90)	Self-care, Home HD or PD (n = 114)	*P* value
TMT B, Median (IQR)	n = 64 102.0 (78.5–132.3)	n = 93 90.0 (63.0–119.0)	0.043[a]
TMT A, Median (IQR)	n = 83 49.0 (32.0–62.0)	n = 110 42.0 (30.0–56.3)	0.029[a]
3MS, Median (IQR)	n = 85 93.0 (88.5–97.0)	n = 108 94.5 (91.0–98.0)	0.063[a]
MCQ1 (metamemory), Mean (SD)	n = 89 17.7 (3.8)	n = 111 17.9 (3.7)	0.61[b]
MCQ2 (metaconcentration), Mean (SD)	n = 88 13.9 (2.4)	n = 110 14.9 (2.8)	0.006[b]
Age, Mean (SD)	62.6 (12.3)	56.8 (13.1)	0.001[b]
Gender, Female	36 (40.0%)	43 (37.7%)	0.74[c]
Education, post-high school	19/87 (21.8%)	32/111 (28.8%)	0.26[c]
Employment			
Retired	51 (56.7%)	48 (42.1%)	
Unemployed	19 (21.1%)	20 (17.5%)	0.022[c]
Salaried/self-employed	20 (22.2%)	46 (40.4%)	
Ethnicity, nonwhite	12 (13.3%)	8 (7.0%)	0.13[c]
Marital status			
Married or partner	56 (62.2%)	76 (66.7%)	
Single	20 (22.2%)	20 (17.5%)	0.86[c]
Divorced or separated	6 (6.7%)	7 (6.1%)	
Widowed	8 (8.9%)	11 (9.6%)	
Cause of ESRD			
Systemic	50 (55.6%)	42 (36.8%)	
Renal	17 (18.9%)	37 (32.5%)	0.020[c]
Other/Unknown	23 (25.6%)	35 (30.7%)	
CCI, Median (IQR)	5.0 (4.0–7.0)	4.0 (3.0–6.0)	0.003[a]
Diabetes	32 (35.6%)	32 (28.1%)	0.25[c]
Heart failure	4 (4.4%)	5 (4.4%)	>0.99[d]
Ischaemic Heart Disease	18 (20.0%)	24 (21.1%)	0.85[c]
IVE	9 (10.0%)	7 (6.1%)	0.31[c]
Urea, Mean (SD)	n = 89 23.3 (7.7)	n = 111 24.0 (6.6)	0.51[b]
Creatinine – Median (IQR)	n = 89 377 (338–459)	n = 111 428 (348–513)	0.013[a]
Hb, <9	3/89 (3.4%)	4/112 (3.6%)	>0.99[d]
Alb, <30	4/89 (4.5%)	2/112 (1.8%)	0.41[d]
Bic	n = 84	n = 110	
<22	37 (44.0%)	49 (44.5%)	
22–28	43 (51.2%)	56 (50.9%)	0.93[e]
>28	4 (4.8%)	5 (4.5%)	
PTH, Median (IQR)	n = 86 23.6 (14.0–35.2)	n = 112 25.2 (13.2–38.2)	0.45[a]
Phosphate	n = 88	n = 111	
<1.1	11 (12.5%)	13 (11.7%)	
1.1–1.7	61 (69.3%)	71 (64.0%)	0.40[e]
>1.7	16 (18.2%)	27 (24.3%)	
SBP, ≤115	4/89 (4.5%)	10/112 (8.9%)	0.22[c]
SBP, Mean (SD)	n = 89 143.7 (19.2)	n = 112 138.4 (20.2)	0.059[b]
DBP, >85	16/89 (18.0%)	21/112 (18.8%)	0.89[c]
DBP, Mean (SD)	n = 89 76.3 (11.1)	n = 112 75.9 (11.6)	0.81[b]
ACEI or ARB	41 (45.6%)	68/112 (60.7%)	0.032[c]
Folic acid	10 (11.1%)	16/112 (14.3%)	0.50[c]
Number of antihypertensive drugs, Median (IQR)	3.0 (2.0–4.0)	n = 112 3.0 (2.0–4.0)	>0.99[a]
EPO	31 (34.4%)	38/113 (33.6%)	0.90[c]
CNS	7 (7.8%)	11/112 (9.8%)	0.61[c]
Antidepressants	18 (20.0%)	13/112 (11.6%)	0.10[c]
Antiplatelets	39 (43.3%)	37/112 (33.0%)	0.13[c]
Statins/EZE	53 (58.9%)	65/112 (58.0%)	0.90[c]
Pill burden, mean (SD)	7.5 (2.6)	n = 112 7.3 (2.9)	0.65[b]
BDI, median (IQR)	n = 82 12.0 (5.8–22.3)	n = 98 7.5 (4.0–13.0)	0.005[a]
STAI State, median (IQR)	n = 80 39.5 (29.3–47.8)	n = 94 32.0 (26.0–42.3)	0.010[a]
STAI Trait, median (IQR)	n = 79 41.0 (30.0–47.0)	n = 91 35.0 (29.0–45.0)	0.049[a]

(Continued)

Table 4. Characteristics of study participants (Continued)

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCI, Charlson Comorbidity Index; CNS, central nervous system; DBP, diastolic blood pressure; EPO, erythropoeitin; ESRD, end-stage renal disease; EZE, ezetemibe; HD, hemodialysis; IQR, interquartile range; MCQI, Metacognition Questionnaire 1; PD, peritoneal dialysis; PTH, parathyroid hormone; SBP, systolic blood pressure; STAI, State and Trait Anxiety Inventory; 3MS, Modified Mini Mental State Examination.
[a]Mann–Whitney *U* test.
[b]Independent-samples *t* test.
[c]Pearson χ^2 test.
[d]Fisher exact test.
[e]χ^2 linear trend test.

to a rational, well–thought-through decision in a hypothetical context. In the choice of self-care dialysis, multiple cognitive processes enable the individual to shift perceptions from the chronic predialysis state to an alternative, imagined perspective on treatment dialysis, through culmination of learning experiences from the past, planning, prediction of imagined events, insight, creativity, and emotional responses. The complex neurobiology of cognition in the face of emotion and affective disorders that CKD patients experience is relatively under-researched. However, impairments in cognitive flexibility and contextual abstraction have been found in other conditions, such as Parkinson disease and depression, with regard to goal-directed behavior and adaptive decision making.[35] In a recent publication from our study group, we demonstrated that the lowest tertile of decision-making scores on a decision-making scale was in fact associated with poorer scores on tests of executive brain function.[36]

Our study has attempted to explore the association between measured cognitive deficits and self-care dialysis modality choice. The influence of patients' assessment of how their memory works, and how they judge their own abilities and effectiveness, may predict their choice of dialysis modality; therefore, a pragmatic brief tool to measure subjective cognitive capacity has been studied here.[31] This is the first study of its kind in the dialysis choice context. The data completeness rate for all aspects of the study combined is excellent.

Our findings suggest that greater cognitive ability is associated significantly with greater self-care dialysis

Table 5. Hierarchical regression analysis of cognition variables with modality choice outcome[a]

Variable		Odds ratio (95% CI)	*P* value
First stage (employment, CCI, and BDI)			
Employment	Retired	1 (–)	
	Unemployed	1.12 (0.44, 2.85)	0.41
	Salaried/self-employed	1.68 (0.77, 3.68)	
CCI (per unit increase)		0.85 (0.71, 1.01)	0.066
BDI (per 10-unit increase)		0.67 (0.49, 0.93)	0.018
Second stage (ethnicity and sex)			
Employment	Retired	1 (–)	
	Unemployed	1.35 (0.51, 3.56)	0.30
	Salaried/self-employed	1.88 (0.84, 4.20)	
CCI (per unit increase)		0.83 (0.70, 0.99)	0.038
BDI (per 10-unit increase)		0.69 (0.50, 0.96)	0.029
Ethnicity, nonwhite		0.26 (0.08, 0.90)	0.033
Sex, female		0.86 (0.45, 1.64)	0.65
Third stage (TMT B variable added) 137/220 (62.3%)			
Employment	Retired	1 (–)	0.10
	Unemployed	1.34 (0.42, 4.24)	
	Salaried/self-employed	2.88 (1.08, 7.70)	
CCI (per unit increase)		0.87 (0.71, 1.08)	0.22
BDI (per 10-unit increase)		0.74 (0.50, 1.09)	0.13
Ethnicity, nonwhite		0.13 (0.03, 0.62)	0.010
Sex, female		0.90 (0.42, 1.93)	0.78
TMT B (per 10-s increase)		0.96 (0.90, 1.02)	0.16
Third stage (TMT A variable added) 170/220 (77.3%)			
Employment	Retired	1 (–)	
	Unemployed	1.69 (0.60, 4.76)	0.29
	Salaried/self-employed	1.91 (0.83, 4.37)	
CCI (per unit increase)		0.85 (0.70, 1.02)	0.084
BDI (per 10-unit increase)		0.66 (0.47, 0.94)	0.021
Ethnicity, nonwhite		0.28 (0.08, 0.98)	0.046
Sex, female		0.86 (0.44, 1.69)	0.67
TMT A (per 10-s increase)		0.91 (0.79, 1.05)	0.21
Third-stage (3MS variable added) 172/220 (78.2%)			
Employment	Retired	1 (–)	
	Unemployed	1.44 (0.53, 3.93)	0.53
	Salaried/self-employed	1.61 (0.69, 3.73)	
CCI (per unit increase)		0.85 (0.71, 1.03)	0.097
BDI (per 10-unit increase)		0.66 (0.47, 0.94)	0.020
Ethnicity, nonwhite		0.28 (0.08, 0.97)	0.044
Sex, female		0.85 (0.44, 1.65)	0.63
3MS (per 10 increase in score)		1.59 (0.86, 2.96)	0.14
Third stage (metamemory variable added) 178/220 (80.9%)			
Employment	Retired	1 (–)	0.24
	Unemployed	1.47 (0.55, 3.94)	
	Salaried/self-employed	2.02 (0.90, 4.53)	
CCI (per unit increase)		0.83 (0.69, 0.99)	0.038
BDI (per 10-unit increase)		0.67 (0.48, 0.95)	0.023
Ethnicity, nonwhite		0.26 (0.08, 0.91)	0.035
Gender, Female		0.86 (0.45, 1.64)	0.64
Metamemory (per unit increase in score)		1.01 (0.93, 1.10)	0.80
Third stage (metaconcentration variable added) 175/220 (79.5%)			
Employment	Retired	1 (–)	0.22
	Unemployed	1.49 (0.53, 4.20)	
	Salaried/self-employed	2.09 (0.91, 4.79)	
CCI (per unit increase)		0.79 (0.66, 0.95)	0.013
BDI (per 10-unit increase)		0.75 (0.52, 1.08)	0.12
Ethnicity, nonwhite		0.28 (0.08, 0.99)	0.048
Sex, female		0.82 (0.42, 1.61)	0.56
Metaconcentration (per unit increase in score)		1.20 (1.05, 1.37)	0.008

BDI, Beck Depression Inventory; CI, confidence interval; CCI, Charlson Comorbidity Index; OR, odds ratio; s, second; TMT, Trail Making Test; 3MS, Modified Mini-Mental State.
[a]OR >1 = Self-care modality choice.

modality choice. Patients' self-reported metaconcentration however, is highly significantly associated with self-care dialysis modality choice. None of the 3 measures of objective cognition assessments, however, is statistically significant in the regression models. The objective tests of cognition lack statistical power. The data that are systematically missing because of patients' inability to complete the test indicates that there could potentially have been a statistically significant association if patients had persevered and completed the tests. However, it is to be noted that recruitment and retention of patients in studies of cognition is difficult[27,37] and may pose a major limitation with respect to practical clinical utility.

The metacognition questionnaire captures patients' beliefs about their memory and concentration components of the cognition process, and it is important, as not every functional area of the brain is affected equally in patients. In an otherwise healthy group of elderly patients, 1 study reported that individuals lacking in self-concept show less problem solving, perhaps because they do not think it is worth trying.[38] If cognitive decline is consciously perceived by individuals, they may no longer practice their cognitive skills and may rely on external assistance.[39] Our study does show a statistically significant association of the metaconcentration scores with tests of executive function (TMT B), consistent with another study in the dialysis population.[15] This is not surprising, and it raises the possibility of the metaconcentration measurement as an effective proxy/complement to objective tests of executive brain function. This remains to

Table 6. Association of metacognition scales with objective tests of cognition

Objective cognition test	n	Parameter estimate (95% CI)	*P* value
Adjusted (for CCI, BDI, and education) regressions with metamemory as the outcome			
TMT B (per 10-s increase)	144	−0.09 (−0.19, 0.02)	0.097
TMT A (per 10-s increase)	180	−0.15 (−0.39, 0.08)	0.19
3MS (per 10 score increase)	179	0.33 (−0.66, 1.33)	0.51
Adjusted (for CCI, BDI, and education) regressions with metaconcentration as the outcome			
TMT B (per 10-s increase)	141	−0.10 (−0.17, −0.03)	0.004
TMT A (per 10-s increase)	177	−0.10 (−0.26, 0.06)	0.21
3MS (per 10 score increase)	176	0.43 (−0.26, 1.12)	0.22

BDI, Beck Depression Inventory; CCI, Charlson Comorbidity Index; CI, confidence interval; s, second; TMT, Trail Making Test; 3MS, Modified Mini Mental State Examination.

be validated, and so does the metacognition questionnaire in the population with renal disease.

Other predictors of hospital-based modality choice after adjustment of cognitive status include nonwhite ethnicity and higher BDI and CCI scores. The latter variables are known to be associated with and to adversely affect both executive and global cognitive functions.[40–43]

Cognitive impairment and/or depressive mood in patients with ESRD can affect patient behaviors, attitudes, and compliance.[44,45] In a routine clinical consultation of the predialysis patient in the UK, patients spend considerable lengths of time being assessed physically in preparation for commencement of dialysis. Communication with the health care team is less than ideally placed to identify all but the most obviously cognitively impaired patients. In these instances, depression may coexist or even overlap. Although some units provide their patients with access to psychotherapy, the vast numbers of practitioners may be oblivious to the insidious development of a psychopathological state in their patients. In 1 study involving physicians' estimation of dialysis patients' cognitive ability during clinical consultations, it was found that doctors had a tendency to underestimate the deficiency when it was present, and only 4 of the 21 impaired patients were classified by their doctor as being cognitively impaired.[46] In the same study, doctors could not identify 25.5% of patients who were depressed, and 45% of those depressed were also found to be cognitively impaired. This knowledge is important not only for the decision-making phase but thereafter for dialysis. Unidentified cognitive deficits may explain nonadherence with diet and fluid management, and also disruptive behaviors on the dialysis unit. Many CKD patients also report sleep disturbances, and these can directly affect memory and concentration.[47] In 1 study of CKD-4/5 patients, sleep-disordered breathing was detected in 49.1% of patients.[48] This group also scored poorly on tests of working and verbal memory, attention, and psychomotor speed.

There is also evidence from literature linking age, cognition, and other individual characteristics with health literacy in advanced age.[49] The finding that impaired health literacy in older age is in part a function of cognitive decline even among persons without dementia necessitates interventions to reduce cognitive demands, particularly complex reasoning abilities and memory from patients, inherent in the health literature materials and decision-making aids used by patients with even milder degrees of cognitive impairment. The question of cognition assessment is therefore important today from a research perspective to answer several questions regarding pathophysiology, potential pharmacological and nonpharmacological interventions, the timing of commencement of these interventions, the appropriate manner of monitoring, and the ideal combination of tests, among other factors, notwithstanding the implications of negative tests on patient behavior and the health care team's practice.

Our study has several limitations. The cross-sectional study design does not confirm the causal impact of cognition on the reported choice of modality. The limited data on TMT part B demonstrated the difficulty of lack of "effort" on the patients' and the administrator's part to "try hard" at the neuropsychological tests, making the results of our study show a relatively smaller proportion of predialysis patients as having significant cognitive impairment. Despite the limitations, the study highlights some important practice points. There may be a role for subjective cognition assessment as a measure of patients' ability to undertake self-care tasks. These patients may well need extra support to cope with the burden of the disease.

In conclusion, patients' own perception of their cognitive ability has an important association with self-care modality choice. This may offer a reliable assessment tool in clinical practice to understand patient phenotype. The subjective report of "metaconcentration" is significantly associated with poorer outcome on the Trail Making Test part B, a test of executive brain function. Several areas of unmet need in understanding cognition in kidney disease should provide the basis for future research.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Table S1. Hierarchical regression of multiple imputation data.

Supplementary material is linked to the online version of the paper at http://www.kireports.org.

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