Loss of executive function after dialysis initiation in adults with chronic kidney disease

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The association of dialysis initiation with changes in cognitive function among patients with advanced chronic kidney disease is poorly described. To better define this, we enrolled participants with advanced chronic kidney disease from the Chronic Renal Insufficiency Cohort in a prospective study of cognitive function. Eligible participants had a glomerular filtration rate of 20 ml/min/1.73m^2 or less, or dialysis initiation within the past two years. We evaluated cognitive function by a validated telephone battery at regular intervals over two years and analyzed test scores as *z* scores. Of 212 participants, 123 did not transition to dialysis during follow-up, 37 transitioned to dialysis after baseline, and 52 transitioned to dialysis prior to baseline. In adjusted analyses, the transition to dialysis was associated with a significant loss of executive function, but no significant changes in global cognition or memory. The estimated net difference in cognitive *z* scores at two years for participants who transitioned to dialysis during follow-up compared to participants who did not transition to dialysis was −0.01 (95% confidence interval −0.13, 0.11) for global cognition, −0.24 (−0.51, 0.03) for memory, and −0.33 (−0.60, −0.07) for executive function. Thus, among adults with advanced chronic kidney disease, dialysis initiation was associated with loss of executive function with no change in other aspects of cognition. Larger studies are needed to evaluate cognition during dialysis initiation.

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[13]See the Appendix for the members of the CRIC Study Investigators.

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Cognitive impairment is common among patients receiving maintenance dialysis, with prevalence estimates exceeding 30%, and it may contribute to excess mortality.[1,2] However, the natural history of cognitive impairment in persons with advanced chronic kidney disease (CKD) and the effect of dialysis initiation on cognitive function remain incompletely defined.

Early studies, primarily in younger individuals with few comorbid conditions, reported that cognitive impairment associated with advanced CKD could be improved by dialysis therapy,[3,4] supporting the hypothesis that metabolites retained in kidney failure and removed by dialysis contributed to impaired cognitive function. These studies had small samples and did not always include controls, making it difficult to determine whether changes in cognitive function were due to dialysis initiation or learning effects from repeated administration of cognitive function tests.

Over the past few decades, the average age and comorbidity burden of patients starting dialysis have increased. In addition, dialysis is now initiated earlier in the course of CKD (i.e., at higher levels of estimated glomerular filtration rate [eGFR]). Concurrent with these changes in demographics and practice, the predominant form of cognitive impairment may no longer be primarily attributable to retained metabolites but rather may be related to cerebrovascular disease and vascular dementia.[1,5,6] If cerebrovascular disease is the principal factor contributing to

cognitive impairment, then dialysis initiation would not be expected to improve cognitive function and might even have deleterious effects.[7,8]

Using data collected from the Chronic Renal Insufficiency Cohort Cognition (CRIC COG) study, we aimed to evaluate the trajectory of cognitive function in a contemporary cohort of adults with advanced CKD before and after dialysis initiation. The CRIC COG study is well- suited to address these questions because its prospective design reduces selection and survival biases. We hypothesized that dialysis initiation would be associated with an accelerated decline in cognitive function.

RESULTS

Participant characteristics

Of the 212 participants included in the cohort, 123 (58%) did not transition to dialysis during follow-up, 37 (17%) transitioned to dialysis after baseline, and 52 (25%) transitioned to dialysis before baseline. The mean age of the cohort was 64.0 ± 10.5 years, 50.9% were male, 46.7% were white, and 57.6% had diabetes. Among participants who were not receiving dialysis at baseline, the mean eGFR was 21.3 ± 7.7 ml/min per 1.73 m^2. Among participants receiving dialysis at baseline, the mean number of months on dialysis was 11.6 ± 7.6. Compared with participants not receiving dialysis at baseline, participants receiving dialysis had slightly lower baseline cognitive test scores (Table 1 and Supplementary Table S1).

On average, participants completed 3.1 ± 1.7 cognitive assessments over 1.4 ± 0.7 years (median, 2.0; interquartile range, 0.8–2.0). The mean absolute change in eGFR from baseline to the end of the study or dialysis initiation was −1.7 ± 8.9 ml/min per 1.73 m^2 for participants who did not transition to dialysis and −7.5 ± 6.3 ml/min per 1.73 m^2 for participants who transitioned to dialysis. In analyses adjusted for age, sex, race, and education, transition to dialysis was associated with a loss of executive function ($P = 0.01$) (Table 2), and no significant changes in global cognition ($P = 0.81$) or memory ($P = 0.12$). These cognitive trajectories are depicted in Figure 1. In sensitivity analyses excluding participants who transitioned to dialysis before baseline, the results were similar (Supplementary Table S2). Transition to dialysis was associated with a loss of executive function ($P = 0.01$) and no significant changes in global cognition ($P = 0.69$) or memory ($P = 0.30$). The sensitivity analysis results were also unchanged after adjustment for baseline eGFR.

The estimated net difference in cognitive function at 2 years for participants who transitioned to dialysis during follow-up compared with participants who did not transition to dialysis was −0.01 (95% confidence interval −0.13 to 0.11) for global cognition, −0.24 (95% confidence interval −0.51 to 0.03) for memory, and −0.33 (95% confidence interval −0.60 to 0.07) for executive function (Figure 2).

Participants who transitioned to dialysis before baseline had slightly larger net differences in cognitive function than participants who transitioned after baseline.

Table 1 | Characteristics of participants with advanced CKD at baseline, stratified by dialysis transition status

Participant characteristics	Did not transition to dialysis (n = 123)	Transitioned to dialysis after baseline (n = 37)	Transitioned to dialysis before baseline (n = 52)	P Value
Age, yr[a]	64.7 ± 10.4	64.5 ± 10.5	62.0 ± 11.0	0.29
Male	63 (51.2)	16 (43.2)	29 (55.8)	0.51
Black race	54 (43.9)	19 (51.4)	40 (76.9)	<0.001
College education	82 (66.7)	27 (73.0)	26 (50.0)	0.05
Diabetes mellitus	65 (52.9)	25 (67.6)	32 (61.5)	0.23
Hypertension	120 (97.6)	37 (100.0)	52 (100.0)	0.33
Previous cardiovascular disease	47 (38.2)	15 (40.5)	19 (36.5)	0.93
Current smoker	12 (9.8)	6 (16.2)	6 (11.5)	0.55
eGFR, ml/min per 1.73 m^2[a]	22.8 ± 7.3	16.1 ± 6.6	—	<0.001
Systolic blood pressure, mm Hg	131 ± 22	140 ± 21	127 ± 22	0.02
Diastolic blood pressure, mm Hg	70 ± 12	72 ± 13	66 ± 11	0.06
No. of months receiving dialysis at baseline	—	—	11.6 ± 7.6	—
Dialysis modality during follow-up[b]				—
Hemodialysis	—	29 (78.4)	43 (82.7)	
Peritoneal dialysis	—	8 (21.6)	10 (19.2)	
Cognitive domain z score[c]				
Global	0.1 ± 0.7	0.1 ± 0.7	−0.2 ± 0.7	0.01
Memory	−0.1 ± 1.7	0.1 ± 1.3	−0.7 ± 2.0	0.08
Executive function	0.2 ± 1.6	−0.002 ± 1.5	−0.1 ± 1.6	0.60

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.
Results are presented as N (%) unless otherwise noted.
[a]Mean ± SD.
[b]Participants may have had more than 1 dialysis modality.
[c]Higher z scores indicate better cognitive function.