

## Cognitive Impairment in Non-Dialysis-Dependent CKD and the Transition to Dialysis: Findings From the Chronic Renal Insufficiency Cohort (CRIC) Study

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**Background:** Advanced chronic kidney disease is associated with elevated risk for cognitive impairment. However, it is not known whether and how cognitive impairment is associated with planning and preparation for end-stage renal disease.

**Study Design:** Retrospective observational study.

**Setting & Participants:** 630 adults participating in the CRIC (Chronic Renal Insufficiency Cohort) Study who had cognitive assessments in late-stage CKD, defined as estimated glomerular filtration rate  $\leq 20$  mL/min/1.73 m<sup>2</sup>, and subsequently initiated maintenance dialysis therapy.

**Predictor:** Predialysis cognitive impairment, defined as a score on the Modified Mini-Mental State Examination lower than previously derived age-based threshold scores. Covariates included age, race/ethnicity, educational attainment, comorbid conditions, and health literacy.

**Outcomes:** Peritoneal dialysis (PD) as first dialysis modality, preemptive permanent access placement, venous catheter avoidance at dialysis therapy initiation, and preemptive wait-listing for a kidney transplant.

**Measurements:** Multivariable-adjusted logistic regression.

**Results:** Predialysis cognitive impairment was present in 117 (19%) participants. PD was the first dialysis modality among 16% of participants (n = 100), 75% had preemptive access placed (n = 473), 45% avoided using a venous catheter at dialysis therapy initiation (n = 279), and 20% were preemptively wait-listed (n = 126). Predialysis cognitive impairment was independently associated with 78% lower odds of PD as the first dialysis modality (adjusted OR [aOR], 0.22; 95% CI, 0.06-0.74; *P* = 0.02) and 42% lower odds of venous catheter avoidance at dialysis therapy initiation (aOR, 0.58; 95% CI, 0.34-0.98; *P* = 0.04). Predialysis cognitive impairment was not independently associated with preemptive permanent access placement or wait-listing.

**Limitations:** Potential unmeasured confounders; single measure of cognitive function.

**Conclusions:** Predialysis cognitive impairment is associated with a lower likelihood of PD as a first dialysis modality and of venous catheter avoidance at dialysis therapy initiation. Future studies may consider addressing cognitive function when testing strategies to improve patient transitions to dialysis therapy.

Complete author and article information (including a list of the CRIC Study Investigators) provided before references.

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Numerous consensus guidelines promote strategies to improve patients' transitions from chronic kidney disease (CKD) to end-stage renal disease (ESRD), including individualized decision making about a preferred dialysis modality, preemptive placement of appropriate dialysis access, and early assessment of eligibility for the kidney transplant waiting list.<sup>1-3</sup> However, underuse of home dialysis therapies such as peritoneal dialysis (PD),<sup>4</sup> widespread use of venous catheters,<sup>1</sup> and the low prevalence of preemptive wait-listing<sup>5</sup> indicate that the transition to dialysis therapy remains suboptimal for many patients. Although prior studies have observed variation across different patient subgroups in achieving these important outcomes,<sup>5-9</sup> whether cognitive impairment contributes to the likelihood of optimal transition to ESRD remains unknown.

Despite recognition that CKD is associated with increased risks for cognitive impairment, cognitive deficits

are frequently underdiagnosed in clinical settings.<sup>10-13</sup> CKD-associated cognitive impairment commonly manifests as diminished executive function and delayed memory,<sup>14</sup> and patients with these deficits may have diminished abilities to focus, plan, retain new knowledge, and complete tasks that are crucial to achieving optimal preparation for ESRD.<sup>15,16</sup>

Therefore, the goal of this study was to evaluate whether differences in predialysis cognitive function may contribute to variation in ESRD transition outcomes. Among participants enrolled in the Chronic Renal Insufficiency Cohort (CRIC) Study who reached late-stage CKD and initiated maintenance dialysis therapy, we assessed the independent association of predialysis cognitive impairment with the likelihood of 4 outcomes: PD as a first dialysis modality, preemptive permanent access placement, avoidance of venous catheter use at dialysis therapy initiation, and preemptive wait-listing for a kidney transplant.

## Methods

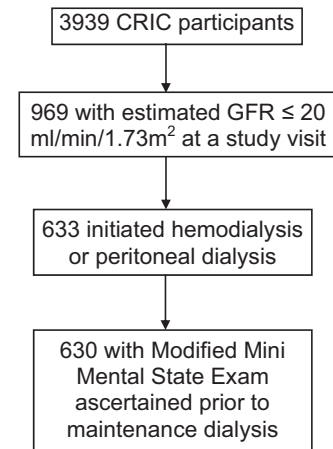
### Study Population

The CRIC Study is an ongoing multicenter prospective study of risk factors for CKD progression and cardiovascular disease. The design and methods of the study and inclusion criteria for study participants have been described previously.<sup>17,18</sup> Briefly, the CRIC Study recruited 3,939 participants aged 21 to 74 years with estimated glomerular filtration rates (eGFRs) in the range of 20 to 70 mL/min/1.73 m<sup>2</sup> from 2003 through 2008. All participants provided informed consent. Participants completed questionnaires at enrollment about socio-demographic information and medical history and returned for yearly visits, during which time this information was updated. All questionnaires remained confidential and for research purposes and were offered in English and Spanish, corresponding to participants' native language and preference. The study protocol was approved by institutional review boards of all participating centers (University of Pennsylvania [coordinating center] IRB protocol #807882), and all research practices are in accordance with the Declaration of Helsinki.

Given evidence that lower levels of kidney function are associated with increased risks for cognitive impairment,<sup>19-21</sup> in the current analyses, we focused on the association of cognitive impairment and ESRD transition outcomes among CRIC participants who initiated dialysis therapy after progression to late-stage CKD. Therefore, we restricted our study to CRIC participants who had a CRIC visit with an eGFR that was  $\leq 20$  mL/min/1.73 m<sup>2</sup> using the Modification of Diet in Renal Disease (MDRD) Study equation.<sup>22</sup> This eGFR threshold was chosen because it is also the cutoff for kidney transplant waiting list eligibility in the United States (see Fig 1, Participant Flow Diagram).<sup>23</sup> We defined the visit with the qualifying eGFR as the index visit.

### Primary Exposure: Predialysis Cognitive Impairment

We ascertained predialysis cognitive function by performance on the Modified Mini-Mental State (3MS) examination. The 3MS, a test of global cognitive function including components that test memory, orientation, concentration, language, and praxis,<sup>24</sup> was administered at baseline and during annual or biannual CRIC visits. 3MS scores range from 0 to 100, with higher scores indicative of better cognitive function. We included the 3MS score for each participant that was closest in time to the index visit and before dialysis therapy onset. We then considered 2 previously recognized strategies to define predialysis cognitive impairment among individuals with CKD based on 3MS performance.<sup>25,26</sup> In our primary analysis, we defined cognitive impairment as 3MS scores lower than previously derived age-based threshold scores<sup>25,27</sup>: <85 for participants younger than 65 years, <80 for participants aged 65 to 79 years, and <75 for those 80 years or



**Figure 1.** Participant inclusion flow diagram. Abbreviations: GFR, glomerular filtration rate; CRIC, Chronic Renal Insufficiency Cohort.

older. In secondary analyses, we examined the association of scores more than 1 standard deviation below the cohort mean score (3MS score < 80)<sup>26,28</sup> on ESRD transition outcomes.

### Covariates

Because our goal was to assess the independent relationship of cognitive impairment with ESRD transition outcomes, we selected covariates a priori for our multivariable models that are commonly used in clinical practice for risk assessment. From the CRIC enrollment visit, we used participant self-reported sex, race/ethnicity, annual household income, educational attainment, and marital status (as a metric of social support). We also included information on the following self-reported medical conditions: diabetes, cardiovascular disease, peripheral vascular disease, congestive heart failure, stroke, and nonskin cancer. At the index visit, we ascertained age (in years), systolic and diastolic blood pressure (in mm Hg), body mass index (in kg/m<sup>2</sup>), tobacco use, and functional status measured by the Kidney Disease Quality of Life Survey Short Form Physical Component Scale.<sup>29</sup> We used laboratory measures from the enrollment and index visit to calculate the slope of eGFR decline before the cognitive assessment visit (mL/min/1.73 m<sup>2</sup> per year) and included serum albumin and serum hemoglobin values (both in g/dL) collected at the index visit.

### Outcomes

We evaluated 4 ESRD transition outcomes: (1) PD as the first dialysis modality, (2) preemptive permanent access placement, (3) venous catheter avoidance at dialysis therapy initiation, and (4) preemptive placement on the transplant waiting list. We defined permanent access as an arteriovenous fistula, graft, or PD catheter. We verified the date and modality of dialysis therapy initiation, presence of a maturing permanent access at dialysis therapy initiation,

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