Kidney Medicine

Body Composition Changes Following Dialysis Initiation and Cardiovascular and Mortality Outcomes in CRIC (Chronic Renal Insufficiency Cohort): A Bioimpedance Analysis Substudy

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Rationale & Objective: Bioelectrical impedance analysis (BIA) provides a noninvasive assessment of body composition. BIA measures of nutritional (phase angle) and hydration (vector length) status are associated with survival among individuals with chronic kidney disease (CKD), including those receiving maintenance dialysis. However, little is known regarding changes in these parameters with CKD following the high-risk transition to maintenance dialysis.

Study Design: Observational study.

Settings & Participants: 427 adults enrolled in the Chronic Renal Insufficiency Cohort (CRIC) Study, with BIA measurements performed within 1 year before and after initiation of maintenance dialysis.

Exposures: We calculated the changes in vector length and phase angle for patients with CKD transitioning to maintenance dialysis.

Outcomes: We examined the association of changes in vector length and phase angle during the transition to maintenance dialysis with risk for all-cause mortality or nonfatal myocardial infarction, stroke, or heart failure, adjusting for demographics, comorbid conditions, and nutritional parameters.

Results: Mean age was 58 ± 12 years and mean estimated glomerular filtration rate using the CKD Epidemiology Collaboration equation before dialysis initiation was 17.0 ± 8.7 mL/min/1.73 m^2. After covariate adjustment, mean changes in vector length and phase angle were 18 (95% CI, 7 to 30) Ω/m and −0.6 (95% CI, −1.3 to 0.1), respectively. Changes in both BIA parameters were not associated with risk for heart failure, stroke, myocardial infarction, or all-cause mortality: HR, 1.02 (95% CI, 0.91-1.14) per 1-SD increment in change for vector length and HR, 1.11 (95% CI, 0.88-1.41) per 1-SD increment in change for phase angle.

Limitations: Observational study, relatively small sample size.

Conclusions: In a multicenter cohort of patients with CKD who progressed to kidney failure, the transition to maintenance dialysis was associated with changes in body composition reflecting poorer cellular integrity and improved volume control. However, these longitudinal changes were not associated with adverse clinical events after dialysis initiation.

Visual Abstract included

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The transition from nondialysis chronic kidney disease (CKD) to maintenance dialysis is a high-risk period associated with adverse patient outcomes. Annual mortality rates during the transition from late-stage CKD through the first year after dialysis initiation exceed 20%.[1] Malnutrition and volume overload are highly prevalent at the time of dialysis initiation, and the presence of these risk factors is associated with adverse outcomes after starting dialysis.[2-9] However, routine clinical measures of health and volume status are largely subjective; the addition of objective measures of body composition and tissue hydration status could help inform clinical decision making.

Bioelectrical impedance analysis (BIA) is a noninvasive portable tool that effectively assesses body composition and offers insights into nutritional and fluid status.[10-13] BIA determines the electrical impedance, or the opposition to an electrical current flow, through body tissues and measures resistance, which is inversely proportional to total body water, and reactance, which is proportional to intracellular mass. Several approaches to BIA analysis have been developed, including regression equations to estimate total body water and other body compartments, or derivations of the measured resistance and reactance at 1 or several frequencies to calculate phase angle (the arc tangent of the reactance to resistance ratio, calculated in radians, and multiplied by 180/π to convert to degrees) and vector length (calculated from the height-adjusted reactance and resistance). Narrow phase angle is associated with malnutrition and poor cellular health,[14-17] whereas foreshortened vector length is a reflection of soft tissue overhydration and associates with clinical parameters of volume overload.[18-21] In both nondialysis CKD and prevalent dialysis populations, narrow phase angle and foreshortened vector length are associated with poorer survival.[12,19,22-24] However, little is known regarding changes in phase angle and vector length during the transition period from nondialysis CKD to maintenance dialysis. If there are meaningful changes in these measures, it is possible that they can be used as surrogate markers to guide therapies during the transition to dialysis.

We sought to examine changes in phase angle and vector length with dialysis initiation among patients with nondialysis CKD enrolled in the Chronic Renal

PLAIN-LANGUAGE SUMMARY

Bioelectrical impedance analysis (BIA) provides a noninvasive assessment of body composition. BIA measures of nutritional (phase angle) and hydration (vector length) status are associated with survival among individuals with kidney disease. However, little is known regarding changes in these parameters during the high-risk transition from nondialysis chronic kidney disease (CKD) to dialysis. In this multicenter cohort of patients with CKD who progressed to dialysis, we found that the transition to maintenance dialysis was associated with changes in body composition reflecting poorer cellular integrity and improved volume control. However, these longitudinal changes were not associated with adverse clinical events after dialysis initiation.

Insufficiency Cohort (CRIC) Study. We further examined the associations of changes in phase angle and vector length with a composite cardiovascular (CV) end point (all-cause mortality or nonfatal myocardial infarction [MI], stroke, or heart failure [HF]).

METHODS

Study Population

This is an ancillary study of CRIC, a multicenter prospective study of adults with mild to moderate CKD that enrolled 3,939 participants between June 2003 and August 2008 at 7 clinical centers across the United States.[25,26] The CRIC Study enrolled participants with Modification of Diet in Renal Disease (MDRD) Study equation–based estimated glomerular filtration rates (eGFRs) between 20 and 70 mL/min/1.73 m^2 for ages 21 to 44 years, 20 to 60 mL/min/1.73 m^2 for ages 45 to 64 years, and 20 to 50 mL/min/1.73 m^2 for ages 65 to 74 years.[27] Inclusion and exclusion criteria have been previously described.[25] Patients receiving maintenance dialysis and kidney transplant recipients were excluded from participation in CRIC, although some participants developed kidney failure and either received dialysis or underwent kidney transplantation during the course of follow-up. CRIC also excluded participants with advanced HF, defined as New York Heart Association class III or IV, on cohort entry. All study participants provided written informed consent, and the study protocol was approved by institutional review boards at each of the participating sites.

CRIC participants returned for annual follow-up visits during which they underwent BIA measurements and were queried regarding end-stage kidney disease status (dialysis initiation or kidney transplantation). Of the 1,192 CRIC participants who progressed to end-stage kidney disease during follow-up, we excluded 686 individuals who did not have BIA measures performed within 1 year before (nondialysis CKD) and 1 year after (post–maintenance dialysis initiation) their end-stage kidney disease date. After further excluding 53 individuals who underwent kidney transplantation and 26 individuals with unknown first kidney replacement modality, our final analytic cohort consisted of 427 participants. Participants included in the analysis had lower prevalences of diabetes, HF, and CV disease (CVD) at baseline compared with those who were excluded (Table S1).

BIA Measurements

BIA measurements were performed at baseline and annually during each follow-up visit using a single-frequency Quantum II bioelectrical impedance analyzer (RLJ Systems) with the participant lying supine with arms 30 from the body and legs not in contact with each other. CRIC participants with pacemakers or with amputations did not undergo BIA testing. Reactance and resistance in ohms (Ω) were obtained from the device and used to calculate phase angle and vector length. Phase angle is a derived measurement obtained from the relation between measures of resistance (R) and reactance (Xc): phase angle = (arctangent Xc/R) $\times$ 180/π and is expressed in degrees. Phase angle can range from 0 to 90 ; 0 if the circuit is only resistive (a system with no cell membranes) and 90 if the circuit is only capacitive (a system of membranes with no fluid). Thus, narrow phase angle is linked with poor cellular integrity. Vector length was calculated according to the vector BIA (RXc graph) methodology and expressed in Ω/m[28]; shorter vector length reflects more extensive soft tissue hydration. For the present analysis, we included BIA measures performed within 1 year before and after dialysis initiation. After dialysis initiation, most study visits were conducted on a nondialysis day.

Ascertainment of CV Events and Mortality

Our primary outcome was the composite outcome of all-cause mortality or nonfatal MI, stroke, or HF. Mortality was ascertained by reports from next of kin, retrieval of death certificates or obituaries, review of hospital or outpatient records, and searching Social Security Death vital status and state death files, if available. CRIC participants were queried every 6 months during alternating in-person and telephone visits regarding hospitalizations or CV events. Discharge diagnosis codes were obtained for all hospitalizations and relevant medical records were retrieved for review by at least 2 physicians. Diagnosis of probable or definite MI was based on symptoms consistent with acute ischemia, cardiac biomarker levels, and electrocardiograms as recommended by a consensus statement on the universal definition of MI.[29] Two neurologists reviewed all hospitalizations suggestive of stroke. Our composite outcome included both probable and definite ischemic stroke and was determined by review of pertinent imaging, autopsies, and symptoms.[30] HF events were determined based on clinical symptoms, radiographic

Table 1. Characteristics of Nondialysis CKD Participants by First Dialysis Modality

	Overall (N = 427)	Hemodialysis (N = 362)	Peritoneal Dialysis (N = 65)
Age, y	58 ± 12	59 ± 12	54 ± 14
Women	178 (42%)	145 (40%)	33 (51%)
Race/ethnicity			
White	79 (19%)	56 (15%)	23 (35%)
Black	231 (54%)	199 (55%)	32 (49%)
Other	117 (27%)	107 (30%)	10 (15%)
Education			
<High school	137 (32%)	130 (36%)	7 (11%)
High school graduate	80 (19%)	73 (20%)	7 (11%)
Some college	139 (33%)	103 (28%)	36 (55%)
≥College graduate	71 (17%)	56 (15%)	15 (23%)
Smoking	54 (13%)	47 (13%)	7 (11%)
Diabetes	293 (69%)	260 (72%)	33 (51%)
Hypertension	420 (98%)	356 (98%)	64 (98%)
Congestive heart failure	56 (13%)	49 (14%)	7 (11%)
Stroke	59 (14%)	48 (13%)	11 (17%)
Cardiovascular disease	177 (41%)	152 (42%)	25 (38%)
Body mass index, kg/m^2	32.2 ± 7.9	32.5 ± 8.1	30.7 ± 6.7
Systolic blood pressure, mm Hg	144.0 ± 26.0	144.8 ± 26.1	139.2 ± 25.2
Diastolic blood pressure, mm Hg	72.0 ± 14.4	71.4 ± 14.5	75.2 ± 13.2
eGFR, mL/min/1.73 m^2	17.0 ± 8.7	17.2 ± 8.9	16.2 ± 7.5
Protein-creatinine ratio, mg/g Cr	2,665.6 [1,297.9-5,502.8]	2,833.1 [1,318.3-5,810.3]	2,016.3 [1,000.4-4,063.5]
Serum albumin, mg/dL	3.5 ± 0.5	3.5 ± 0.6	3.6 ± 0.5
Baseline hsCRP, mg/L	2.5 [1.0-6.4]	2.5 [1.0-6.6]	2.7 [0.9-5.6]
Baseline LDL cholesterol, mg/dL	105.2 ± 41.5	104.9 ± 41.1	107.0 ± 44.3
Baseline HDL cholesterol, mg/dL	45.2 ± 15.0	44.9 ± 15.1	46.9 ± 14.6
Diuretics	315 (74%)	271 (75%)	44 (68%)
ACEis/ARBs	234 (55%)	186 (51%)	48 (74%)
β-Blockers	277 (65%)	244 (67%)	33 (51%)
Lipid-lowering medications	292 (68%)	243 (67%)	49 (75%)

Note: Values given as mean ± standard deviation, number (percent), or median [interquartile range]. Conversion factors for units: Cholesterol in mg/dL to mmol/L, × 0.02586.
Abbreviations: ACEi/ARB, angiotensin-converting enzyme/angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

evidence of pulmonary edema, physical examination of heart and lungs, central venous hemodynamic monitoring data, and echocardiographic imaging.

Ascertainment of Covariates

Trained CRIC Study staff collected participants' self-reported sociodemographic and medical histories during the baseline visit. CVD included any history of coronary artery disease, MI, HF, stroke, and peripheral vascular disease. Current medications were ascertained using the inventory method.[25,26] Serum creatinine (enzyme-based assay), serum albumin (dye-binding assay), and plasma glucose were measured on the Hitachi Vitros 950 AT. GFR was estimated using the 2009 CKD Epidemiology Collaboration (CKD-EPI) equation ($eGFR_{CKD\text{-}EPI}$).[31] Twenty-four–hour urinary albumin excretion was measured on the Siemens Immulite.[32,33] Diabetes mellitus was defined as fasting glucose level > 126 mg/dL, nonfasting glucose level > 200 mg/dL, or use of insulin/other antidiabetic medications. Blood pressure was obtained at each annual study visit in a standardized setting by trained coordinators.

Statistical Analysis

We tabulated baseline participant characteristics according to levels of vector length and phase angle measured during the nondialysis CKD visit. We calculated changes in vector length and phase angle by taking the difference between post– and pre–maintenance dialysis initiation measurements and adjusted for covariates using a linear mixed model. We further assessed whether changes in vector length and phase angle differed by dialysis modality: hemodialysis (HD) versus peritoneal dialysis (PD). We tested the correlation of changes in phase angle and vector length with changes in weight, body mass index (BMI), and serum albumin level. We tested the univariate associations of participant characteristics with odds of change in phase angle and vector length using logistic regression models.

We used Cox regression to estimate associations of change in phase angle and vector length (predictor, modeled

Table 2. Pre– and Post–Maintenance Dialysis Initiation Vector Length and Phase Angle

	Unadjusted		Model 1		Model 2	
	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*
Vector length (Ω/m)						
Nondialysis CKD mean	434 (424 to 444)		434 (425 to 443)		437 (429 to 444)	
Postdialysis mean	478 (469 to 488)		478 (469 to 487)		455 (444 to 466)	
Absolute change (post- − predialysis)	44 (36 to 53)	<0.001	44 (36 to 53)	<0.001	18 (7 to 30)	0.002
Phase angle, °						
Nondialysis CKD mean	6.9 (6.5 to 7.2)		6.9 (6.5 to 7.2)		6.8 (6.5 to 7.2)	
Postdialysis mean	6.2 (5.8 to 6.5)		6.2 (5.8 to 6.5)		6.3 (5.7 to 6.8)	
Absolute change (post- − predialysis)	−0.7 (−1.2 to −0.2)	0.007	−0.7 (−1.2 to −0.2)	0.008	−0.6 (−1.3 to 0.1)	0.09

Note: Model 1 adjusted for age, sex, race, and clinical site. Model 2 adjusted for model 1 plus history of heart failure, any cardiovascular disease, stroke, diabetes, smoking, estimated glomerular filtration rate according to CKD Epidemiology Collaboration equation, urinary albumin-creatinine ratio, systolic blood pressure, serum albumin level, and weight. *P* value tests the difference in the absolute change (post- − predialysis). Adjusted estimates adjust for mean values of all covariates.
Abbreviation: CKD, chronic kidney disease.

continuously) with the composite outcome, with follow-up time starting from the BIA measurement after initiating maintenance dialysis. For all analyses, we adjusted for potential confounders including age, sex, race, and clinical site (model 1) and added further adjustments for history of HF, any CVD, stroke, diabetes, smoking, $eGFR_{CKD\text{-}EPI}$, urinary albumin-creatinine ratio, systolic blood pressure, and serum albumin level (model 2). For the linear mixed model, we treated all covariates as time varying. For the time-to-event model, we adjusted for covariates from the post–dialysis initiation visit, except for $eGFR_{CKD\text{-}EPI}$, which was ascertained from the pre–dialysis initiation visit for both models. We further adjusted for baseline vector length and phase angle (model 3) for the time-to-event model. In a secondary analysis, changes in phase angle and vector length were modeled in tertiles and the Cox models as described were repeated.

A nominal $P < 0.05$ was taken as evidence of statistical significance in all analyses. All analyses were conducted using the R, version 3.6.0, computing environment (R Foundation for Statistical Computing).

RESULTS

Description of the Study Population

Among the 427 study participants, mean age was 58 ± 12 years, 42% were women, 19% were White, and 54% were Black. Mean nondialysis CKD $eGFR_{CKD\text{-}EPI}$ was 17.0 ± 8.7 mL/min/1.73 m^2 (Table 1). A total of 69% of study participants reported a history of diabetes, and 98% reported a history of hypertension. Most study participants were treated with HD rather than PD (85% vs 15%). Compared with patients receiving PD, patients receiving HD tended to be older, were more likely to be Black, were more likely to have diabetes mellitus, and had higher BMI and systolic blood pressure.

Compared with participants within the lowest tertile of nondialysis CKD vector length, those within the highest tertile were more likely to be women, had lower BMI and systolic blood pressure, had fewer medical comorbid conditions, and were more likely to have been initiated on PD (Table S2). Across levels of nondialysis CKD phase angle, participants within the highest tertile were younger, were less likely to be women, had higher BMI, and had fewer comorbid conditions (Table S3).

Changes in Phase Angle and Vector Length Pre– and Post–Dialysis Initiation

The median time between nondialysis CKD and post–dialysis initiation BIA measurements was 395 (interquartile range [IQR], 349-497) days. On average, BIA measures were performed a median of 220 (IQR, 105-314) days before dialysis initiation and a median of 222 (IQR, 103-308) days after dialysis initiation. Mean nondialysis CKD vector length was 434 Ω/m (95% CI, 424-444 Ω/m; Table 2). After adjusting for demographics, comorbid conditions, kidney function measures, and nutritional parameters, mean change in vector length with dialysis initiation was 18 (95% CI, 7-30) Ω/m, indicating improvement in hydration status. Mean nondialysis CKD phase angle was 6.9° (95% CI, 6.5 to 7.2), and after covariate adjustment, mean change in phase angle was −0.6 (95% CI, −1.3 to 0.1), suggesting worsening nutritional status. In sensitivity analyses, changes in vector length and phase angle did not differ by dialysis modality (Table S4). Changes in vector length and phase angle did not correlate strongly with changes in weight, BMI, or serum albumin level from nondialysis CKD to maintenance dialysis (Fig S1).

Participants who were female, were Black, had HF, with higher BMI, lower eGFR, and lower proteinuria were more likely to have a change in vector length in the top 50% of change values. Participants with a history of CVD and higher proteinuria were less likely to have a change in phase angle in the top 50% of change values (Table 3).

Association of Change in Vector Length and Phase Angle With Clinical Outcomes

During a median follow-up period of 5.1 (25th, 75th percentile range, 2.8, 7.6) years, there were 242 events for the composite outcome of HF, stroke, or MI or all-cause

Table 3. Univariate Associations of Clinical Characteristics With Change in BIA Measures During the Transition Period

	Vector Length		Phase Angle	
Variable	**Odds Ratio (95% CI)**	***P***	**Odds Ratio (95% CI)**	***P***
Age (per 10-y increment)	1.05 (0.90-1.24)	0.52	0.93 (0.79-1.10)	0.40
Male sex	0.65 (0.44-0.95)	0.03	0.85 (0.58-1.25)	0.41
Race/ethnicity				
White	1.00 (reference)		1.00 (reference)	
Black	1.89 (1.12-3.19)	0.02	1.03 (0.62-1.72)	0.90
Other	1.66 (0.93-2.97)	0.09	1.22 (0.69-2.15)	0.50
Education				
<High school	1.00 (reference)		1.00 (reference)	
High school graduate	0.76 (0.44-1.32)	0.33	0.47 (0.27-0.83)	0.009
Some college	1.00 (0.62-1.60)	0.99	0.97 (0.60-1.56)	0.90
≥College graduate	0.85 (0.48-1.52)	0.59	0.76 (0.43-1.35)	0.35
Smoking	0.78 (0.44-1.38)	0.39	1.09 (0.62-1.94)	0.76
Diabetes	1.35 (0.89-2.03)	0.15	1.08 (0.72-1.63)	0.70
Hypertension	1.33 (0.29-6.03)	0.71	2.52 (0.48-13.15)	0.27
Congestive heart failure	1.01 (0.57-1.76)	0.99	0.85 (0.49-1.50)	0.58
Stroke	2.17 (1.22-3.87)	0.008	0.89 (0.52-1.55)	0.69
Cardiovascular disease	1.07 (0.73-1.57)	0.74	0.95 (0.65-1.40)	0.80
Body mass index (per 5 kg/m^2 increment)	1.18 (1.04-1.34)	0.008	0.84 (0.74-0.95)	0.006
Systolic blood pressure (per 10 mm Hg increment)	1.17 (1.08-1.27)	0.0001	1.04 (0.97-1.12)	0.27
Diastolic blood pressure (per 5 mm Hg increment)	0.98 (0.92-1.05)	0.63	1.07 (1.00-1.14)	0.06
eGFR (per 15 mL/min/1.73 m^2 increment)	0.89 (0.64-1.24)	0.49	1.07 (0.77-1.48)	0.70
Protein-creatinine ratio, median (mg/g Cr), per doubling	1.25 (1.09-1.44)	0.002	1.09 (0.96-1.24)	0.19
Serum albumin (per 0.5 mg/dL increment)	0.66 (0.55-0.79)	<0.0001	0.82 (0.69-0.97)	0.02
Baseline hsCRP, median (mg/L), per doubling	1.00 (0.76-1.31)	0.99	0.91 (0.68-1.22)	0.54
Baseline LDL cholesterol (per 10 mg/dL increment)	1.01 (0.95-1.07)	0.79	1.04 (0.97-1.11)	0.24
Diuretics	0.86 (0.56-1.32)	0.49	0.96 (0.62-1.48)	0.85
ACEis/ARBs	0.72 (0.49-1.05)	0.09	0.73 (0.50-1.07)	0.11
β-Blockers	1.12 (0.75-1.68)	0.57	1.19 (0.80-1.77)	0.40
Lipid-lowering medications	0.93 (0.62-1.40)	0.73	0.99 (0.65-1.48)	0.94

Note: Entries are the odds of having BIA change in the top 50% of change values. Covariates all measured at pre–end-stage kidney disease visit. Conversion factors for units: Cholesterol in mg/dL to mmol/L, ×0.02586.
Abbreviations: ACEi/ARB, angiotensin-converting enzyme/angiotensin receptor blocker; BIA, bioelectrical impedance analysis; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitivity C-reactive protein.

mortality. In the fully adjusted model, greater changes in both vector length and phase angle between post– and pre–dialysis initiation were associated with higher risk for HF, stroke, MI, or all-cause mortality (Table 4); however, these assocations did not reach statistical significance: hazard ratios, 1.02; 95% CI, (0.91-1.14) per 1-SD increment in change for vector length and 1.11 (95% CI, 0.88-1.41) per 1-SD increment in change for phase angle. Results were similar when change in phase angle and vector length were modeled in tertiles (Table S5).

DISCUSSION

Among 427 individuals from the CRIC Study with non-dialysis CKD who initiated maintenance dialysis during follow-up, phase angle narrowed while vector length extended. Our findings suggest that the initiation of maintenance dialysis is associated with worse cellular integrity (sometimes refered to as "nutritional status") while improving volume status. Last, we did not observe any significant associations of changes in vector length or phase angle with clinical outcomes, although the number of events was relatively low.

Prior work has demonstrated the prognostic importance of phase angle and vector length in kidney disease. Among prevalent patients receiving dialysis, narrower phase angle and foreshortened vector length are associated with higher risk for death independent of comorbid conditions and nutritional markers.[12,19,22-24] In a meta-analysis that pooled data from 4 dialysis cohorts, each degree lower

Table 4. Associations of Longitudinal Change in Vector Length and Phase Angle During Transition From Nondialysis CKD to Maintenance Dialysis With Subsequent Clinical Outcomes

	No. at Risk (no. of events)	Unadjusted (95% CI)	Model 1 (95% CI)	Model 2 (95% CI)	Model 3 (95% CI)
Composite (HF, stroke, MI, or all-cause mortality)					
Change in phase angle					
Per 1-SD increment in change	427 (242)	1.07 (0.98, 1.18)	1.12 (1.02, 1.22)	1.04 (0.94, 1.15)	1.02 (0.91, 1.14)
Change in vector length					
Per 1-SD increment in change	427 (242)	0.96 (0.84, 1.11)	0.94 (0.82, 1.08)	0.98 (0.83, 1.17)	1.11 (0.88, 1.41)

Note: Model 1 adjusted for age, sex, race, and clinical site. Model 2 adjusted for model 1 plus history of HF, any cardiovascular disease, stroke, diabetes, smoking, estimated glomerular filtration rate according to CKD Epidemiology Collaboration equation, urinary albumin-creatinine ratio, systolic blood pressure, serum albumin level, and weight. Model 3 adjusted for model 2 plus baseline vector length or phase angle.
Abbreviations: CKD, chronic kidney disease; HF, heart failure; MI, myocardial infarction.

phase angle was associated with 1.74 times higher risk for death (95% CI, 1.37-2.21).[12]

Our group has also shown similar findings in more than 3,000 CRIC participants with nondialysis CKD.[34] We did not find a significant association between changes in phase angle and vector length in the transition between nondialysis CKD and maintenance dialysis with risk for CVD and mortality. The reasons for this are unclear but could be related to the select population that was studied (which was a healthier population that survived and also participated in study visits) or the timing of the BIA measurements (which were performed annually).

Effective volume management is critical in kidney failure, especially during the high-risk transition period to dialysis. In our study, mean vector length was shorter at advanced CKD compared with similar aged healthy adults, indicating worse hydration status.[35] Individuals with advanced CKD who initiate maintenance dialysis for volume overload experience higher mortality rates compared with those who initiate dialysis for uremic symptoms or laboratory result abnormalities.[6] Among patients new to dialysis, the presence of fluid overload at the time of or shortly following dialysis initiation is associated with increased risk for death.[7,8] Considering the subjective and imprecise nature of physical examintion, an objective tool such as BIA may help assess health and volume status and guide volume management. Our study and prior work suggest that vector length corresponds with volume status changes in maintenance dialysis patients. Among patients receiving in-center HD, mean vector length increased immediately after the HD session.[18,36] In a recent study of more than 1,000 patients new to PD that estimated overall hydration status using bioimpediance parameters, volume overload improved from the onset of dialysis initiation through the first year and remained stable during years 2 and 3.[7]

Few randomized controlled trials have assessed the effects of BIA-guided volume management. Among patients receiving maintenance dialysis, beneficial effects of BIA-guided therapy included improved volume status, decrease in left ventricular mass, and lower blood pressure compared with routine care.[37] Although a trial of 131 HD patients found improvements in overall survival among patients in the BIA arm at 2.5 years of follow-up,[38] a recent trial that followed up 240 patients receiving PD over 1 year showed no differences in CV events or all-cause mortality.[39] Because these studies were limited by modest sample size (and more importantly, the modest number of events) and focused on prevalent dialysis patients, there is a need for large-scale randomized controlled trials to determine whether optimizing volume status using BIA improves clinical outcomes among patients with CKD initiating maintenance dialysis.

Our results also suggest that the progression from nondialysis CKD to dialysis is associated with a modest decline in cellular integrity/nutritional status, highlighting the need for nutritional and possibly other lifestyle interventions during this vulnerable period. Consistent with our findings, prior work has shown that CKD progression is associated with decreased dietary protein intake and decline of other nutritional indexes such as serum albumin level, BMI, and muscle mass.[40,41] In a recent longitudinal study of more than 3,900 CRIC participants, body weight, fat-free mass, and serum albumin level remained stable until eGFR decreased to <35 mL/min and steadily declined thereafter. Faster rate of body weight decline in nondialysis CKD was associated with higher risk for death after dialysis initiation.[2]

However, several studies have demonstrated improvements in nutritional status with dialysis initiation.[42-45] One single-center study of 50 incident HD patients showed improvements in serum albumin level and protein catabolic rate and increase in phase angle (mean, 5.41° vs 6.24°) between the initial dialysis session and at 1 year after starting dialysis.[43] Differences in study populations may account for these discrepant findings. We evaluated patients during the transition period from nondialysis CKD to dialysis, whereas the existing studies examined patients longitudinally after dialysis initiation.

Our study has several strengths. We used data from a diverse and well-characterized cohort of patients with CKD with longitudinal follow-up and were able to adjust for a number of important time-varying confounders. We are

also one of the first studies to examine changes in BIA measurements during the transition period to mainenance dialysis.

We recognize several limiations as well. We did not have data on short-term changes in body weight, residual kidney function, or intradialytic weight gain (only annual measures). Currently, there are no established thresholds to define abnormal phase angle and vector length at 1 time point or longitudinally. The differing lengths of time between BIA measures pre– and post–maintenance dialysis intiation varied across participants, which may have affected our results. The BIA measures were performed annually at study visits; we were not able to evaluate for shorter term changes. CRIC was a study of research volunteers, therefore limiting the external validity of our findings.

In a multicenter cohort of individuals with nondialysis CKD who progressed to kidney failure treated by dialysis, initiation of maintenance dialysis was associated with poorer cellular integrity/nutritional status and improved volume control based on BIA measurements. Therefore, BIA may be an effective tool to help guide clinical management during this high-risk period and improve patient outcomes.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Correlation of changes in vector length and phase angle with changes in routine clinical measures from advanced nondialysis CKD to dialysis

Table S1. Baseline characteristics of CRIC participants who progressed to maintenance dialysis (with HD or PD as first modality), comparing those who were included versus excluded for analysis

Table S2: Demographic characteristics among all maintenance dialysis patients, by tertile of nondialysis CKD vector length

Table S3: Demographic characteristics among all maintenance dialysis patients, by tertile of nondialysis CKD phase angle

Table S4: Baseline and change in vector length and phase angle pre– and post–maintenance dialysis initiation, by dialysis modality

Table S5: Associations of categorical longitudinal changes in vector length and phase angle during transition from nondialysis CKD to maintenance dialysis with subsequent clinical outcomes

ARTICLE INFORMATION

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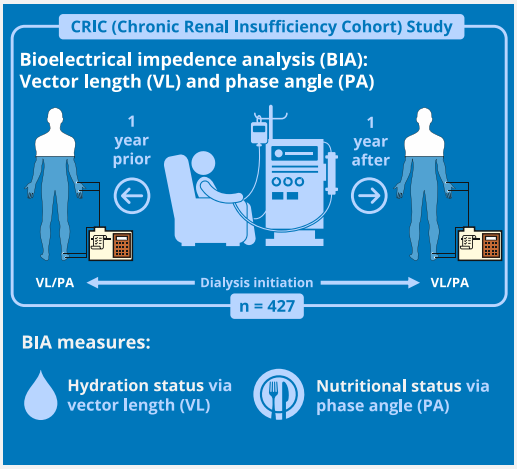
Is the change in bioimpedance measurement after transition from CKD to ESKD associated with hard outcomes?

Kidney Medicine



Findings

58 ± 12 years
Mean age

17.0 ± 8.7
Mean pre-ESKD $eGFR_{CKD-EPI}$

What did BIA show?

18 Ω/m
7 to 30 Ω/m
Vector length
→ Improved hydration status

-0.6°
-1.3 to 0.1°
Phase angle
→ Worsening nutritional status

Changes in BIA parameters were not associated with

- Mortality
- Heart failure
- Stroke
- Myocardial infarction

HR 1.11
0.88-1.41

Conclusion: The transition from CKD to maintenance dialysis was associated with changes in body composition reflecting poorer cellular integrity and improved volume control. However, these longitudinal changes were not associated with adverse clinical events after dialysis initiation.

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