Quality of Life and Risk of Cardiac Events, ESRD, and Death in African Americans with Renal Disease

BY

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THESIS

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LIST OF ABBREVIATIONS

AASK	African American Study of Kidney Disease and Hypertension
CKD	Chronic Kidney Disease
CV	Cardiovascular
eGFR	Estimated Glomerular Filtration Rate
ESRD	End Stage Renal Disease
HMO	Health Maintenance Organization
HRQOL	Health Related Quality of Life
MHC	Mental Health Composite
PHC	Physical Health Composite
SCR	Serum Creatinine
SF-36	Short Form-36
UP/Cr	Urine Protein-Creatinine Ratio

SUMMARY

Health-related quality of life (HRQOL) has been associated with increased risk for hospitalizations and mortality in patients with end stage renal disease (ESRD), but has not been evaluated as a predictor of adverse outcomes in patients with chronic kidney disease (CKD).

A longitudinal analysis examining baseline HRQOL with health outcomes during five years of follow-up was performed, involving 639 African Americans with hypertensive CKD from the African American Study of Kidney Disease and Hypertension (AASK) Cohort Study. Quality of life, including mental health composite (MHC) and physical health composite (PHC), was assessed at study baseline using the Short Form-36 (SF-36). The association between MHC and PHC and the outcomes of kidney disease progression (defined as doubling of serum creatinine or development of ESRD), cardiovascular events, and all-cause mortality was examined.

At baseline, mean (± standard deviation) participant SF-36 MHC and PHC scores were 46.3 ± 10.5 and 40.4 ± 10, respectively. In adjusted analyses, lower baseline PHC score (per 5 unit decrements) was significantly associated with an increased risk of cardiovascular events [1.11 (95% CI 1.00-1.23)] and all-cause mortality [1.13 (95% CI 1.02-1.26)]. There was no independent association between baseline MHC scores and any of the outcomes, nor for baseline PHC scores and the endpoint of kidney disease progression.

Lower baseline SF-36 PHC but not MHC was associated with an increased risk of cardiovascular events and death. Neither PHC nor MHC scores were associated with progression of kidney disease. Future work will need to focus on mechanisms underlying the association between PHC scores and adverse outcomes.

I. INTRODUCTION

Health-related quality of life (HRQOL) has been defined as an individual's "functional status and the subjective state of well being as it is related to one's health condition."[1] HRQOL has increasingly become the focus of research in various chronic illnesses, as the relevance of the impact of illness and treatments on patient-oriented outcomes has gained recognition. In addition, consideration has been given to the idea that poor HRQOL may be associated with negative health outcomes. Previous studies have examined the relationship between HRQOL and clinical outcomes in patients with end-stage renal disease (ESRD) and have found that poor HRQOL is associated with increased mortality.[2,3,4] However, this relationship is less clear in patients with earlier stages of chronic kidney disease (CKD), particularly in African American patients. Furthermore, there is little evidence regarding the relationship between poor HRQOL and progressive renal disease in CKD patients,[5] and this has not been examined in African Americans. Because African Americans are at increased risk of developing ESRD compared to whites,[6] HRQOL and its impact on clinical outcomes within this population deserve better understanding.

This study aims to examine the relationship between baseline measures of HRQOL and subsequent development of doubling of serum creatinine/ESRD, cardiovascular events, and all-cause mortality in a five-year follow-up of a cohort of African Americans with hypertensive chronic kidney disease.

II. METHODS

A. Study Design

We conducted a longitudinal analysis to examine the relationship between baseline measures of quality of life and kidney disease progression, cardiovascular events, and all-cause mortality over five years of follow-up in participants of the African American Study of Kidney Disease and Hypertension (AASK) Cohort Study. The AASK Cohort Study was a multicenter observational study of African Americans with hypertensive chronic kidney disease who had previously participated in the AASK Trial and had not reached death or ESRD requiring dialysis or transplantation at its conclusion. The design and methods of both of these studies have been described previously.[7,8] Out of 764 eligible participants from the AASK Trial, 691 were enrolled in 2002 and followed through 2007. Baseline HRQOL data were available for 639 participants, who comprised the final analytic cohort. All study participants provided written informed consent and the study was approved by the Institutional Review Boards of the participating centers.

B. Variables and Data Sources

Subjects provided demographic and clinical information at enrollment and completed the SF-36 (Short Form-36) quality of life instrument at baseline. The SF-36 is a survey questionnaire with 36 questions that is a generic assessment of quality of life and is used in both healthy and chronically ill populations.[9] This instrument has been used extensively in patients with ESRD and CKD.[10,11,5,12] There are individual scale scores of the following 8 domains: Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE), and Mental Health (MH). These eight scales can be combined as summary measures: Physical Health Composite (PHC) and Mental Health Composite (MHC) with a mean score of 50 in the general population.[13]

Sociodemographic variables including age, gender, marital status, income, insurance status, and level of education were reported by participants at study enrollment. Participants also reported comorbid medical conditions at study enrollment. Clinical variables such as blood pressure measurements were obtained in a standardized

fashion. Estimated GFR was calculated using the AASK Study Equation[14] and urine protein-creatinine ratio was measured at a single laboratory by standard methods.

C. Outcomes

Primary outcomes were a renal composite outcome consisting of doubling of serum creatinine or development of end-stage kidney disease, a cardiovascular composite consisting of cardiovascular events or cardiovascular mortality, and all-cause mortality. Cardiovascular events were identified as any of the following events: myocardial infarction, new-onset or worsened coronary heart disease, new-onset or worsened congestive heart failure, and cerebrovascular accident. Each cardiovascular event was adjudicated by the Cardiovascular Outcome Committee to determine if events met the definition outlined in the study protocol. The criteria defining each of these events have been reported previously.[15] For each death event, the clinical centers informed the coordinating centers of the primary and secondary cause of death listed on the participant death certificate.

D. Statistical Methods

Participants' baseline mean (± standard deviation (SD)) and quartiles of PHC and MHC scores were described according to categories of demographic and clinical characteristics. For each primary outcome, event rates were calculated as the ratio of the number of patients reaching the event divided by the total patient-years of follow-up before an event or until censoring. Follow-up time for the cardiovascular composite was censored at ESRD or transplantation occurrence or non-cardiovascular death, and follow-up time for the ESRD/doubling of serum creatinine composite was censored at all-cause death. Kaplan-Meier curves were created to represent the cumulative probability of each of the three primary outcomes. Cox regression models were used to assess the association between each of the three primary outcomes and baseline PHC or MHC. The statistical analyses were performed with Unix SAS version 8.2 (Cary, NC, USA).

III. RESULTS

A. Participants and Characteristics

Of 691 participants who enrolled in the cohort study, 639 completed the SF-36 at baseline (92.5%). Mean participant age was 60 years at the start of the study, and 61% were male. Forty-two percent of the participants reported an annual household income below $15,000 and 35% were unemployed. The mean BMI at baseline was 31.4 ± 7.1 kg/m^2. The mean baseline blood pressure was 136/81 (±22/12) mmHg. The average estimated GFR was 43.8 ± 17 ml/min/1.73 m^2 and average urine protein level was 0.38 ± 0.85 g/g (urinary protein-creatinine ratio).

B. Sociodemographic and Clinical Characteristics by Baseline HRQOL Scores

The mean MHC score was 40.4 ± 10 and the mean PHC score was 46.3 ± 10.5 for the cohort at baseline. Higher quartiles of MHC scores were associated with male gender, employment, higher categories of income, and having private health insurance ($p< 0.05$, Table 1). Higher quartiles of PHC scores were associated with employment, higher categories of income, and private health insurance ($p<0.05$, Table 3). Lower quartiles of MHC scores were associated with history of peripheral vascular disease and lower baseline GFR ($p< 0.05$, Table 2). Lower quartiles of PHC scores were associated with higher diastolic BP, higher baseline serum creatinine, history of cardiovascular disease, history of stroke, history of peripheral vascular disease, lower baseline GFR, and higher baseline urinary protein-creatinine ratio ($p<0.05$, Table 4).

TABLE I
GENERAL SOCIODEMOGRAPHIC CHARACTERISTICS OF AASK COHORT PARTICIPANTS AT BASELINE BY MHC QUARTILE

	All Patients (N=639)	MHC < 39 (N=143)	MHC 39-48 (N=172)	MHC 48-55 (N=163)	MHC 55+ (N=161)	
Variable	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	p
Age (years)	60.0 ± 10.2	58.3 ± 9.17	59.5 ± 10.7	61.2 ± 9.46	60.8 ± 11.0	0.05
Gender (% Male)	396 (62.0%)	76 (53.1%)	108 (62.8%)	97 (59.5%)	115 (71.4%)	0.01
Marital Status						0.26
Never Married	114 (17.9%)	27 (18.9%)	34 (19.8%)	23 (14.1%)	30 (18.8%)	
Married/Married-like Relationship	235 (36.8%)	46 (32.2%)	56 (32.6%)	68 (41.7%)	65 (40.6%)	
Divorced or Separated	194 (30.4%)	51 (35.7%)	59 (34.3%)	42 (25.8%)	42 (26.3%)	
Widow/Widower	95 (14.9%)	19 (13.3%)	23 (13.4%)	30 (18.4%)	23 (14.4%)	
Lives Alone	190 (29.8%)	44 (30.8%)	54 (31.4%)	46 (28.2%)	46 (28.8%)	0.91
Employment Status						<0.01
Employed	235 (36.8%)	34 (23.8%)	57 (33.1%)	75 (46.0%)	69 (43.1%)	
Full-time homemaker	16 (2.5%)	4 (2.8%)	5 (2.9%)	4 (2.5%)	3 (1.9%)	
Retired	225 (35.3%)	43 (30.1%)	69 (40.1%)	52 (31.9%)	61 (38.1%)	
Unemployed	97 (15.2%)	38 (26.6%)	26 (15.1%)	19 (11.7%)	14 (8.8%)	
Student	1 (0.2%)			1 (0.6%)		
Other	64 (10.0%)	24 (16.8%)	15 (8.7%)	12 (7.4%)	13 (8.1%)	
Annual Income ($)						0.01
< $15,000	268 (42.0%)	77 (53.8%)	71 (41.3%)	65 (39.9%)	55 (34.4%)	
$15,000-$39,999	168 (26.3%)	29 (20.3%)	52 (30.2%)	41 (25.2%)	46 (28.8%)	
$40,000+	66 (10.3%)	9 (6.3%)	12 (7.0%)	19 (11.7%)	26 (16.3%)	
Declines to Answer	136 (21.3%)	28 (19.6%)	37 (21.5%)	38 (23.3%)	33 (20.6%)	
Health Insurance						0.01
Private/HMO/Other	196 (30.7%)	44 (30.8%)	49 (28.5%)	60 (36.8%)	43 (26.9%)	
Medicaid/Medicare Only	255 (40.0%)	69 (48.3%)	74 (43.0%)	57 (35.0%)	55 (34.4%)	
None of the Above	187 (29.3%)	30 (21.0%)	49 (28.5%)	46 (28.2%)	62 (38.8%)	

TABLE II
GENERAL CLINICAL CHARACTERISTICS OF AASK COHORT PARTICIPANTS
BY BASELINE MHC QUARTILE

	All Patients (N=639)	MHC < 39 (N=143)	MHC 39-48 (N=172)	MHC 48-55 (N=163)	MHC 55+ (N=161)	
Variable	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	p
Weight (kg)	92.1 ± 22.4	94.1 ± 25.5	92.5 ± 21.6	91.7 ± 21.3	90.5 ± 21.3	0.57
Body Mass Index (kg/m^2)	31.4 ± 7.10	32.1 ± 8.13	31.6 ± 6.69	31.4 ± 6.80	30.7 ± 6.84	0.36
Systolic BP (mm Hg)	136 ± 22.0	138 ± 22.6	136 ± 24.1	133 ± 19.5	135 ± 21.6	0.34
Diastolic BP (mm Hg)	80.8 ± 12.4	82.2 ± 12.9	81.7 ± 12.8	80.2 ± 12.1	79.4 ± 11.9	0.17
Serum Creatinine (mg/dL)	2.30 ± 1.32	2.49 ± 1.54	2.22 ± 1.44	2.35 ± 1.20	2.16 ± 1.05	0.13
History of CV Disease	137 (21.5%)	48 (33.6%)	37 (21.5%)	30 (18.4%)	22 (13.8%)	<0.01
History of Stroke	116 (18.2%)	27 (18.9%)	36 (20.9%)	34 (20.9%)	19 (11.9%)	0.11
History of Peripheral Vascular Disease	36 (5.6%)	14 (9.8%)	11 (6.4%)	7 (4.3%)	4 (2.5%)	0.04
Estimated GFR (AASK Equation)	43.7 ± 16.7	41.6 ± 18.2	45.5 ± 16.3	41.5 ± 16.6	46.1 ± 15.3	0.02
Urine Protein/Creatinine	0.39 ± 0.85	0.51 ± 1.02	0.38 ± 0.87	0.37 ± 0.79	0.30 ± 0.71	0.21

TABLE III
GENERAL SOCIODEMOGRAPHIC CHARACTERISTICS OF AASK COHORT PARTICIPANTS AT BASELINE BY PHC QUARTILE

	All Patients (N=639)	PHC < 33 (N=157)	PHC 33-42 (N=145)	PHC 42-49 (N=174)	PHC 49+ (N=163)	
Variable	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	p
Age (years)	60.0 ± 10.2	60.1 ± 9.67	60.5 ± 9.75	60.2 ± 9.72	59.3 ± 11.5	0.76
Gender (% Male)	396 (62.0%)	93 (59.2%)	80 (55.2%)	117 (67.2%)	106 (65.0%)	0.11
Marital Status						0.612
Never Married	114 (17.9%)	24 (15.4%)	29 (20.0%)	27 (15.5%)	34 (20.9%)	
Married/Married-like Relationship	235 (36.8%)	53 (34.0%)	50 (34.5%)	68 (39.1%)	64 (39.3%)	
Divorced or Separated	194 (30.4%)	57 (36.5%)	41 (28.3%)	52 (29.9%)	44 (27.0%)	
Widow/Widower	95 (14.9%)	22 (14.1%)	25 (17.2%)	27 (15.5%)	21 (12.9%)	
Lives Alone	190 (29.8%)	51 (32.7%)	45 (31.0%)	55 (31.6%)	39 (23.9%)	0.30
Employment Status						<0.01
Employed	235 (36.8%)	23 (14.7%)	49 (33.8%)	83 (47.7%)	80 (49.1%)	
Full-time homemaker	16 (2.5%)	3 (1.9%)	7 (4.8%)	4 (2.3%)	2 (1.2%)	
Retired	225 (35.3%)	67 (42.9%)	52 (35.9%)	58 (33.3%)	48 (29.4%)	
Unemployed	97 (15.2%)	35 (22.4%)	26 (17.9%)	17 (9.8%)	19 (11.7%)	
Student	1 (0.2%)				1 (0.6%)	
Other	64 (10.0%)	28 (17.9%)	11 (7.6%)	12 (6.9%)	13 (8.0%)	
Annual Income ($)						<0.01
< $15,000	268 (42.0%)	89 (57.1%)	61 (42.1%)	65 (37.4%)	53 (32.5%)	
$15,000-$39,999	168 (26.3%)	38 (24.4%)	33 (22.8%)	46 (26.4%)	51 (31.3%)	
$40,000+	66 (10.3%)	5 (3.2%)	17 (11.7%)	21 (12.1%)	23 (14.1%)	
Declines to Answer	136 (21.3%)	24 (15.4%)	34 (23.4%)	42 (24.1%)	36 (22.1%)	
Health Insurance						<0.01
Private/HMO/Other	196 (30.7%)	35 (22.4%)	43 (29.7%)	61 (35.1%)	57 (35.0%)	
Medicaid/Medicare Only	255 (40.0%)	88 (56.4%)	61 (42.1%)	61 (35.1%)	45 (27.6%)	
None of the Above	187 (29.3%)	33 (21.2%)	41 (28.3%)	52 (29.9%)	61 (37.4%)	

TABLE IV
GENERAL CLINICAL CHARACTERISTICS OF AASK COHORT PARTICIPANTS
BY BASELINE PHC QUARTILE

	All Patients (N=639)	PHC < 33 (N=157)	PHC 33-42 (N=145)	PHC 42-49 (N=174)	PHC 49+ (N=163)	
Variable	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	n (%) or mean ± s.d.	p
Weight (kg)	92.1 ± 22.4	94.4 ± 24.4	93.2 ± 24.1	91.5 ± 20.6	89.7 ± 20.5	0.27
Body Mass Index (kg/m^2)	31.4 ± 7.10	32.0 ± 7.87	32.2 ± 6.76	31.1 ± 6.88	30.7 ± 6.80	0.19
Systolic BP (mm Hg)	136 ± 22.0	139 ± 23.3	136 ± 22.3	133 ± 22.2	135 ± 20.1	0.14
Diastolic BP (mm Hg)	80.8 ± 12.4	83.0 ± 12.9	81.0 ± 12.8	78.9 ± 11.6	80.7 ± 12.3	0.03
Serum Creatinine (mg/dL)	2.30 ± 1.32	2.46 ± 1.42	2.47 ± 1.71	2.22 ± 1.08	2.08 ± 0.96	0.02
History of CV Disease	137 (21.5%)	62 (39.7%)	26 (17.9%)	26 (14.9%)	23 (14.1%)	<0.01
History of Stroke	116 (18.2%)	35 (22.4%)	33 (22.8%)	28 (16.1%)	20 (12.3%)	0.04
History of Peripheral Vascular Disease	36 (5.6%)	20 (12.8%)	8 (5.5%)	5 (2.9%)	3 (1.8%)	<0.01
Estimated GFR (AASK Equation)	43.7 ± 16.7	41.5 ± 17.7	42.2 ± 18.1	44.2 ± 15.5	46.7 ± 15.2	0.03
Urine Protein/Creatinine	0.39 ± 0.85	0.52 ± 1.10	0.45 ± 0.96	0.26 ± 0.49	0.34 ± 0.76	0.03

C. Cumulative Incidence of Outcomes

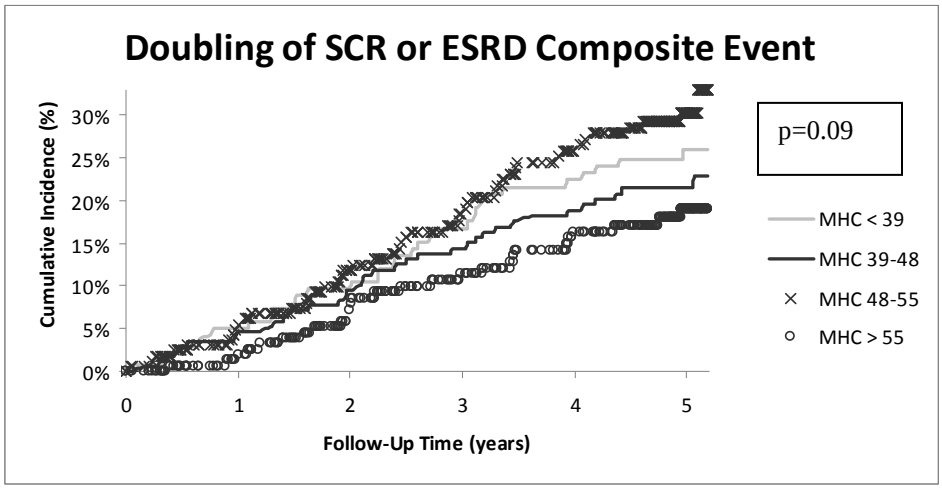
The mean follow-up time for ESRD/doubling of serum creatinine was 48.7 months, for cardiovascular events was 47.7 months, and for death was 54.7 months. There were a total of 96 cardiovascular events and 143 participants reached ESRD/doubling of serum creatinine during the period of follow-up. Ninety-nine participants died during the period of follow-up. The cumulative incidence rate of cardiovascular events and all-cause mortality was significantly higher for lower quartiles of PHC (p=0.003 and p=0.01, respectively) (Table 5, Figure 2). There was no significant difference between the cumulative incidence rates for any of the outcomes by MHC quartiles or for doubling of serum creatinine/ESRD by PHC quartiles (p>0.05) (Table 5, Figure 1).

TABLE V
CUMULATIVE INCIDENCE AND RATE OF DOUBLING OF SCR/ESRD, CARDIOVASCULAR EVENTS AND DEATH BY QUARTILE OF BASELINE MHC AND PHC

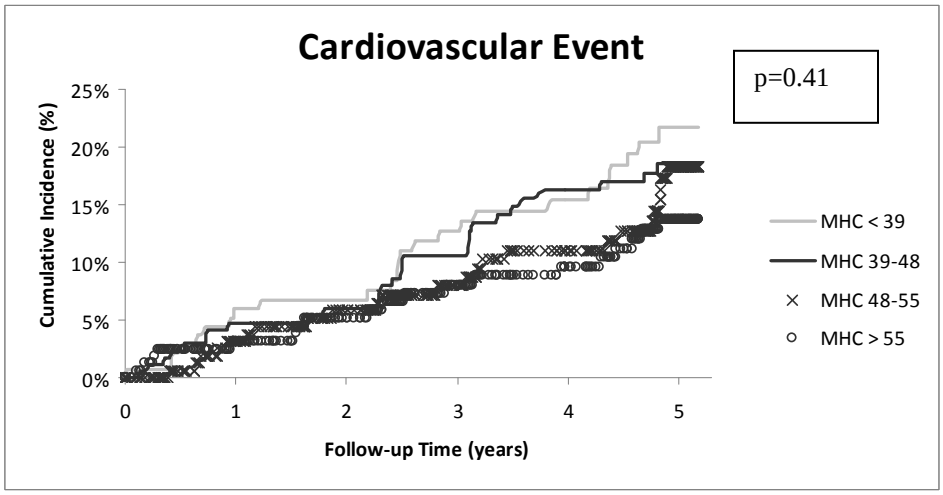
		CV Composite Event			Doubling of SCR/ESRD			All-Cause Mortality		
MHC Quartile	N	# Events	Percent	Rate / 100 pt years	# Events	Percent	Rate / 100 pt years	# Events	Percent	Rate / 100 pt years
< 39	143	25	17.48	4.72	33	23.08	5.99	26	18.18	4.14
39-48	172	28	16.28	4.04	36	20.93	5.04	23	13.37	2.86
48-55	163	24	14.72	3.68	47	28.83	7.20	21	12.88	2.77
55+	161	19	11.80	2.87	27	16.77	4.04	29	18.01	4.03
PHC Quartile	N	# Events	Percent	Rate/100 pt years	# Events	Percent	Rate/100 pt years	# Events	Percent	Rate/100 pt years
< 33	157	34	21.66	6.03	37	23.57	6.39	34	21.66	5.07
33-42	145	24	16.55	4.39	41	28.28	7.35	26	17.93	3.98
42-49	174	22	12.64	3.05	37	21.26	4.94	20	11.49	2.42
49+	163	16	9.82	2.27	28	17.18	4.00	19	11.66	2.51

Figure 1. Cumulative Incidence of (a) Doubling of Serum Creatinine/ESRD, (b) Cardiovascular Events, and (c) Death by Quartile of MHC Score.

a)



b)



c)

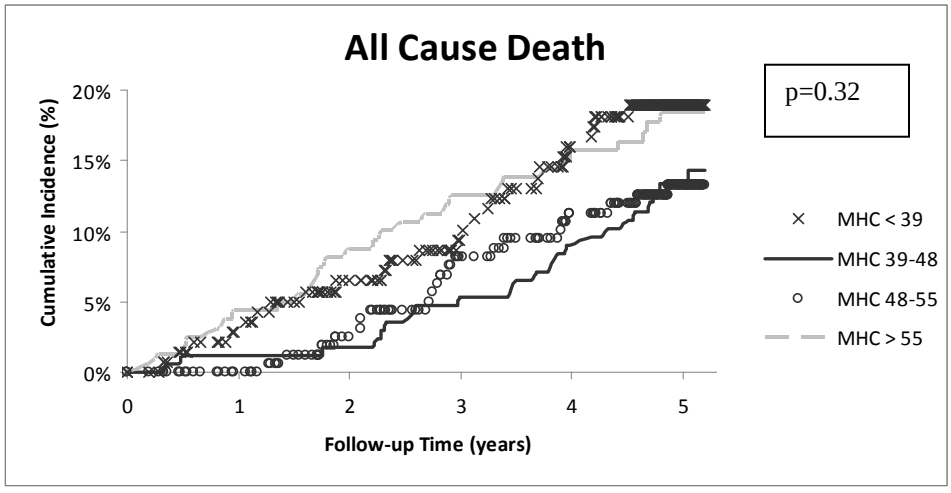
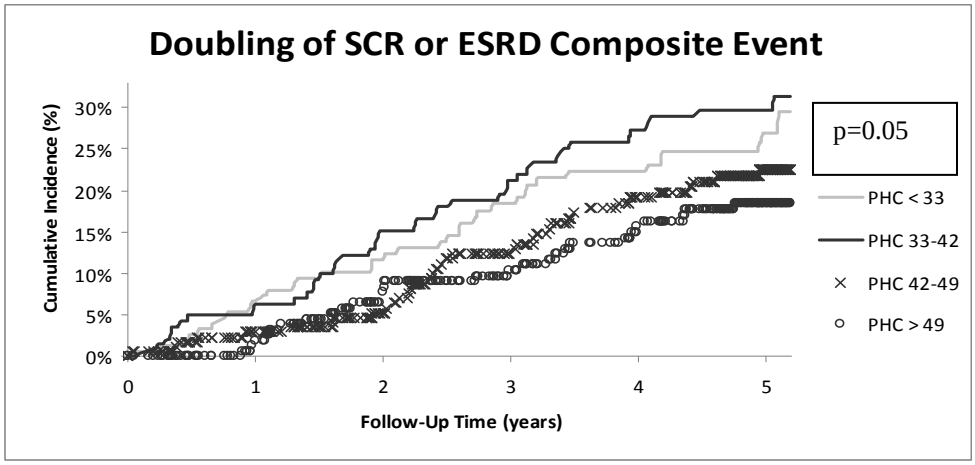


Figure 2. Cumulative Incidence of (a) Doubling of Serum Creatinine/ESRD, (b) Cardiovascular Events, and (c) Death by Quartile of PHC Score.

a)



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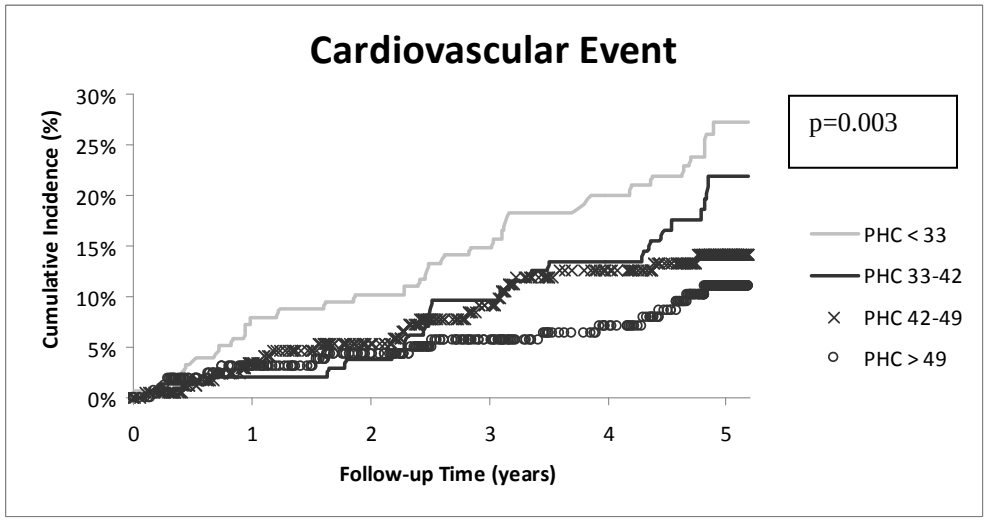

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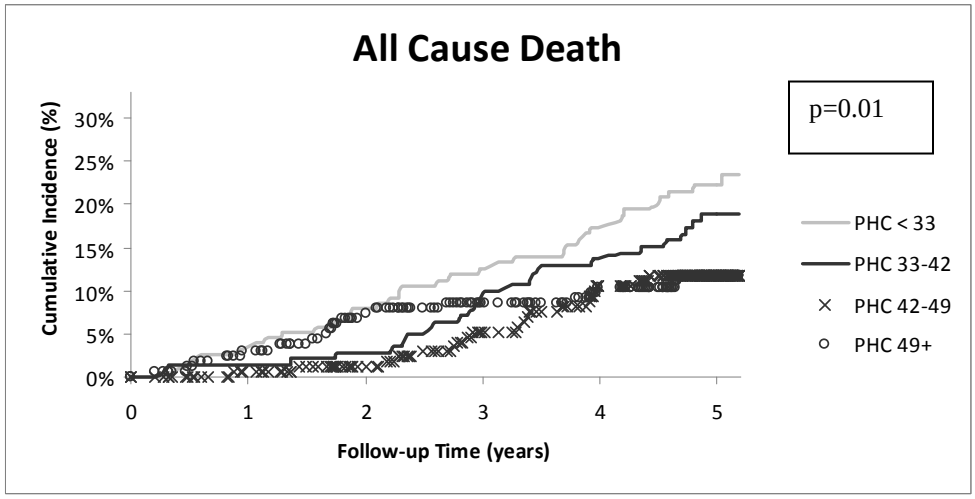

D. Relative Risks of Outcomes by 5-Point Increment of HRQOL Scores

The unadjusted relative risk of cardiovascular events increased by 1.19 for each 5-point decrease in PHC score (95% confidence interval 1.08-1.30, p=0.001, Table 6). The relative risk for CV events remained increased by 1.11 for each 5-point decrease in PHC score after adjustment for age, gender, baseline eGFR, proteinuria, and history of cardiovascular disease (95% confidence interval 1.00-1.23, p=0.04). In adjusted analysis, the relative risk of all-cause mortality was 1.13 for each 5-point decrease in PHC (95% confidence interval 1.02-1.26, p=0.02). The relative risk of doubling of serum creatinine/ESRD was not statistically significantly different for each 5-point decrement in PHC. For each of the three outcomes, the relative risk for each 5-point decrement in MHC was not statistically significantly different in unadjusted or adjusted analyses (p>0.05, Table 6).

TABLE VI
ASSOCIATION BETWEEN BASELINE MHC AND PHC AND DOUBLING OF SCR/ESRD, CARDIOVASCULAR COMPOSITE, AND DEATH (PER 5-POINT LOWER MHC OR PHC SCORE)

MHC Analyses	Unadjusted	P	Adjusted 1[a]	p	Adjusted 2[b]	p
Cardiovascular composite	1.09 (0.99, 1.20)	0.07	1.09 (0.99, 1.20)	0.07	1.03 (0.93, 1.13)	0.61
Kidney disease composite	1.05 (0.97, 1.13)	0.22	1.02 (0.94, 1.10)	0.63	0.98 (0.91, 1.07)	0.67
All death	1.00 (0.91, 1.10)	0.94	1.02 (0.92, 1.13)	0.72	1.00 (0.90, 1.12)	0.93
PHC Analyses	Unadjusted	P	Adjusted 1[a]	p	Adjusted 2[b]	p
Cardiovascular composite	1.19 (1.08, 1.30)	<0.01	1.18 (1.07, 1.30)	<0.01	1.11 (1.00, 1.23)	0.04
Kidney disease composite	1.08 (0.99, 1.17)	0.07	1.01 (0.93, 1.09)	0.90	0.99 (0.90, 1.07)	0.74
All death	1.16 (1.06, 1.28)	<0.01	1.13 (1.02, 1.25)	0.02	1.13 (1.02, 1.26)	0.02

[a] For adjusted analysis 1, covariates include age, gender, baseline eGFR .

[b] For adjusted analysis 2, covariates include age, gender, baseline eGFR, UP/Cr and history of CVD.

E. Relative Risks of Outcomes by Quartiles of HRQOL Scores

When the adjusted relative risk of each of the outcomes was examined by quartiles of HRQOL scores, participants with scores in the lowest PHC quartile were found to have an increased risk of 1.99 relative to those in the highest PHC quartile for cardiovascular events (95% confidence interval 1.08-3.70, Table 8). Adjusted relative risk of doubling of serum creatinine/ESRD and all-cause mortality were not significantly different by quartile of PHC score and adjusted relative risks of any of the three outcomes were not significantly different by quartile of MHC score (Table 7).

TABLE VII
ADJUSTED RELATIVE RISKS OF DOUBLING OF SCR/ESRD, CARDIOVASCULAR EVENTS, AND DEATH BY MHC QUARTILES

	Doubling of SCr/ESRD	CV composite	Death
Highest quartile (>55)	1.0	1.0	1.0
2nd quartile (48-55)	1.43 (0.88, 2.34)	1.21 (0.66, 2.22)	0.58 (0.33, 1.04)
3rd quartile (39-48)	1.35 (0.80, 2.28)	1.40 (0.78, 2.52)	0.72 (0.41, 1.27)
4th quartile (<39)	1.17 (0.69, 1.97)	1.65 (0.90, 3.02)	1.07 (0.62, 1.87)
Highest quartile (>55)[a]	1.0	1.0	1.0
2nd quartile (48-55)	1.36 (0.82, 2.23)	1.12 (0.61, 2.07)	0.60 (0.33, 1.07)
3rd quartile (39-48)	1.12 (0.65, 1.91)	1.12 (0.62, 2.05)	0.68 (0.38, 1.23)
4th quartile (<39)	0.95 (0.55, 1.63)	1.17 (0.62, 2.20)	1.01 (0.56, 1.80)

[a] Shaded area represents the results adjusted for age, gender, baseline eGFR, UP/Cr and history of CVD.

TABLE VIII
ADJUSTED RELATIVE RISKS OF DOUBLING OF SCR/ESRD, CARDIOVASCULAR EVENTS, AND DEATH BY PHC QUARTILES

	Doubling of SCr/ESRD	CV composite	Death
Highest quartile (>49)	1.0	1.0	1.0
2nd quartile (42-49)	1.15 (0.70, 1.91)	1.33 (0.70, 2.55)	0.90 (0.48, 1.71)
3rd quartile (33-42)	1.51 (0.91, 2.50)	1.88 (0.99, 3.54)	1.32 (0.72, 2.43)
4th quartile (<33)	1.20 (0.72, 1.98)	2.69 (1.48, 4.90)	1.71 (0.95, 3.05)
Highest quartile (>49)[a]	1.0	1.0	1.0
2nd quartile (42-49)	1.39 (0.83, 2.32)	1.37 (0.71, 2.62)	0.97 (0.51, 1.86)
3rd quartile (33-42)	1.52 (0.92, 2.52)	1.65 (0.86, 3.17)	1.33 (0.71, 2.47)
4th quartile (<33)	1.11 (0.66, 1.87)	1.99 (1.08, 3.70)	1.72 (0.94, 3.17)

[a] Shaded area represents the results adjusted for age, gender, baseline eGFR, UP/Cr and history of CVD.

IV. DISCUSSION

This study provides evidence that low baseline PHC scores are associated with increased risk for cardiovascular events and all-cause mortality in African Americans with hypertensive CKD, but not with doubling of serum creatinine/ESRD. In this study, MHC scores were not associated with any of these clinical outcomes.

Previous studies of ESRD patients have demonstrated that poor HRQOL is associated with an increased risk of mortality.[2,16,3,4] However, there has been a lack of studies in patients with earlier stages of CKD demonstrating similar findings. One large cohort study in an elderly Korean population including participants with and without CKD demonstrated that the effect of low HRQOL on mortality is exaggerated in those with CKD compared to those without CKD after adjustment for other variables,[17] suggesting a disproportionate burden of low HRQOL on health in CKD patients. This is the first study to our knowledge of the association between baseline HRQOL and renal, cardiovascular, and mortality events in a population of patients with earlier-stage CKD.

Our study did not find an association between HRQOL and renal outcomes. Previous studies have been conflicting with respect to this clinical outcome. A study by Fukuhara et al in a cohort of Japanese patients with CKD stages III and IV found that decreases in HRQOL over time were associated with increases in creatinine of 1 mg/dL.[5] The differences in our findings may relate to the larger decrement in renal function used as an endpoint in our study (doubling of serum creatinine, vs. a 1 mg/dL increase in the Fukuhara study), or to differences in the patient populations involved in the studies.

The mechanisms underlying the association between PHC scores and cardiovascular events and all-cause mortality are unclear, and it is also not clear why a similar relationship between MHC scores and clinical outcomes is not observed. Previous studies have suggested that PHC scores are a marker of physical function,[18,19] and low physical function has been shown to be associated with increased mortality.[20] In addition, possible mechanisms that may underlie the association between poor HRQOL and increased mortality and cardiovascular events include treatment-compliance related factors such as adherence to medications and physician visits,[21] or the negative effect

of poor self-perceived health and its associated stress on cardiovascular, metabolic, and immunologic function, leading to negative health consequences.[22]

There are several limitations to the study. Our study only included African Americans with hypertensive CKD, which may limit generalizability to patients with other causes of CKD and other racial/ethnic groups. However, because African Americans with hypertensive CKD are a large population at particular risk of progression to ESRD,[23,6,24] the findings of this study may be commonly applied in clinical practice. Second, this study does not assess the mechanism underlying the association between HRQOL and negative clinical outcomes.

In conclusion, low PHC, but not MHC, is associated with increased risk of cardiovascular events and all-cause mortality in a cohort of African Americans with CKD. Neither PHC nor MHC was associated with increased risk of doubling of serum creatinine/ESRD. This study highlights the association between poor HRQOL and negative clinical outcomes in a pre-ESRD population and suggests the need for future studies to determine the mechanisms underlying this association and for interventions to improve HRQOL and thus clinical outcomes.

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