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CLINICAL RESEARCH

Self-reported Medication Adherence and CKD Progression

Esteban A. Cedillo-Couvert[1], Ana C. Ricardo[1], Jinsong Chen[1], Janet Cohan[1], Michael J. Fischer[1,8,9], Marie Krousel-Wood[2], John W. Kusek[3], Swati Lederer[1,8,9], Eva Lustigova[2], Akinlolu Ojo[4], Anna C. Porter[1], Lisa K. Sharp[1], James Sondheimer[5], Clarissa Diamantidis[6], Xue Wang[7], Jason Roy[7] and James P. Lash[1]; on behalf of the CRIC Study Investigators[10]

[1]Department of Medicine, University of Illinois at Chicago, Chicago, Ilinois, USA; [2]Department of Medicine and Epidemiology, Tulane University, New Orleans, Louisiana, USA; Research Division, Ochsner Health System, New Orleans, Louisiana, USA; [3]National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland, USA; [4]Department of Medicine, University of Arizona, Phoenix, Arizona, USA; [5]Department of Internal Medicine, Wayne State University, Detroit, Michigan, USA; [6]Department of Medicine, Duke University School of Medicine, Durham, North Carolina, USA; [7]Department of Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, Pennsylvania, USA; [8]Department of Medicine, Jesse Brown VAMC, Chicago, Illinois, USA; and [9]Research Service, Center of Innovation for Complex Chronic Healthcare, Edward Hines Jr., VA Hospital, Hines, Illinois, USA

Introduction: In the general population, medication nonadherence contributes to poorer outcomes. However, little is known about medication adherence among adults with chronic kidney disease (CKD). We evaluated the association of self-reported medication adherence with CKD progression and all-cause death in patients with CKD.

Methods: In this prospective observational study, 3305 adults with mild-to-moderate CKD enrolled in the Chronic Renal Insufficiency Cohort (CRIC) Study. Baseline self-reported medication adherence was assessed by responses to 3 questions and categorized as high, medium, and low. CKD progression (50% decline in eGFR or incident end-stage renal disease) and all-cause death were measured using multivariable Cox proportional hazards.

Results: Of the patients, 68% were categorized as high adherence, 17% medium adherence, and 15% low adherence. Over a median follow-up of 6 years, there were 969 CKD progression events and 675 deaths. Compared with the high-adherence group, the low-adherence group experienced increased risk for CKD progression (hazard ratio = 1.27, 95% confidence interval = 1.05, 1.54) after adjustment for sociodemographic and clinical factors, cardiovascular medications, number of medication types, and depressive symptoms. A similar association existed between low adherence and all-cause death, but did not reach standard statistical significance (hazard ratio = 1.14 95% confidence interval = 0.88, 1.47).

Conclusion: Baseline self-reported low medication adherence was associated with an increased risk for CKD progression. Future work is needed to better understand the mechanisms underlying this association and to develop interventions to improve adherence.

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Medication nonadherence has been recognized as a major barrier to disease treatment and contributes to disease progression, death, and increased health care costs in the United States.[1] Medication nonadherence in patients with chronic conditions is common, with rates across studies averaging 50% and higher.[2–5] Moreover, an association between low medication adherence and increased risk of adverse clinical outcomes has been reported among patients with diabetes mellitus, hypertension, coronary artery disease, heart failure, and HIV.[6–10]

It is estimated that more than 26 million individuals in the United States have chronic kidney disease (CKD).[11] The progression of CKD to end-stage renal disease (ESRD) is associated with high rates of

Correspondence: Esteban A. Cedillo-Couvert, Division of Nephrology, Department of Medicine, 820 South Wood Street, M/C 793, Chicago, Illinois 60612, USA. E-mail: ecedillo@uic.edu

[10]The Chronic Renal Insufficiency Cohort (CRIC) Study Group investigators include Lawrence J. Appel, Harold I. Feldman, Alan S. Go, Jiang He, John W. Kusek, James P. Lash, Mahboob Rahman, Panduranga S. Rao, and Raymond R. Townsend.

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morbidity and mortality and increased health care costs.[12] Despite the magnitude of this problem and evidence suggesting that risk factor control is an important determinant of CKD progression,[13] very little is known regarding the impact of medication adherence on CKD progression. To address this knowledge gap, we used data from the prospective Chronic Renal Insufficiency Cohort (CRIC) Study to evaluate the association of self-reported medication adherence with CKD progression and all-cause death. We hypothesized that low medication adherence would be associated with higher risk for CKD progression among persons with CKD.

METHODS

Study Participants

The CRIC Study is an ongoing multicenter, prospective, observational study of risk factors for CKD and cardiovascular disease progression. The design, methods and baseline characteristics of study participants have been previously described.[14–16] From 2003 to 2008, the study recruited 3939 adult participants aged 21 to 74 years with an estimated glomerular filtration rate (eGFR) of 20 to 70 ml/min per 1.73 m^2 at 7 clinical centers in the United States. Exclusion criteria included individuals unable to provide consent, institutionalized, pregnant, and with certain severe chronic conditions.[14] Self-reported medication adherence was evaluated at the year-1 study visit, which was considered to be the baseline for this study. Figure 1 delineates the derivation of the study population. The study protocol adhered to the Declaration of Helsinki and was approved by the institutional review boards of participating centers. All participants provided written informed consent.

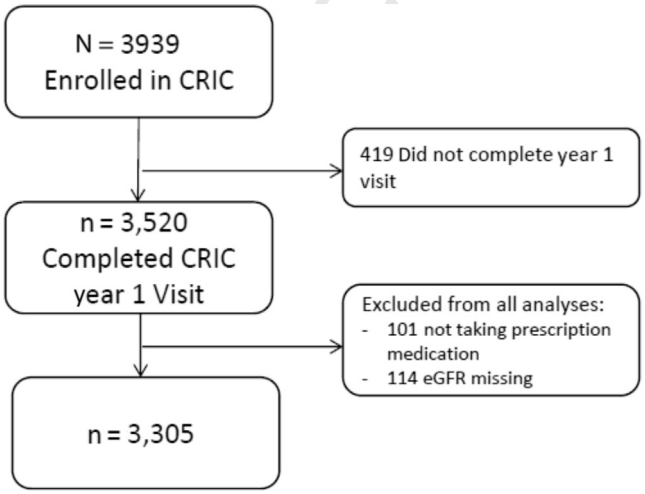

Figure 1. Analytic cohort flow chart. CRIC, Chronic Renal Insufficiency Cohort; eGFR, estimated glomerular filtration rate.

Measurements

Information about sociodemographic variables, medical history, psychosocial factors, and medications were obtained by self-report. Height, weight, and waist circumference were measured.[15] Body mass index was calculated as weight in kilograms divided by height in meters squared. At each annual clinic visit, 3 seated blood pressure (BP) measurements were obtained using a Tycos Classic Hand Aneroid cuff and sphygmomanometer (Welch Allyn) following a standardized protocol. The mean of all BP measurements was used as the BP value for that visit. Hypertension was defined as mean BP $\geq$ 140/90 mm Hg or use of antihypertensive medication. Hemoglobin A1c (HbA1c) was measured using high-performance liquid chromatography (BioRad, Hercules, CA). Diabetes was defined as fasting plasma glucose of $\geq$126 mg/dl or use of insulin or oral hypoglycemic medications. Depressive symptoms were assessed using the Beck Depression Inventory (BDI), and a score of $\geq$11 was considered to be indicative of clinically meaningful depressive symptoms based on a recent study in CKD patients.[17] GFR was estimated annually using a CRIC-specific equation.[18] A 24-hour urine sample collected at study entry was used to measure urine protein and creatinine.

Predictor

Medication adherence was assessed based on the responses to 3 questions as follows: (i) "In the past week, how many days did you forget to take a pill?" (ii) "In the past week, how many days did you not take a pill on purpose?" (iii) "In the past week, how many days did you add an extra pill?"[19,20] The 3 possible responses to each question were: 0 days, 1 day, and 2 days or more. These 3 items were used in a study by Choo *et al.*[19] Because this is not a validated questionnaire and there is no scoring system for these items, we derived our own approach to scoring. We ranked forgetting to take a pill as the least significant form of nonadherence, and purposefully not taking a medicine or adding a medication as the most significant forms of nonadherence, based on a prior study that used a modified version of these questions.[20] We divided the score into 3 adherence categories: high, medium, and low. Individuals with a response of "0 days" to all 3 items were categorized as high adherence; individuals reporting only forgetting a pill at least 1 day in the past week were categorized as medium adherence; and individuals who reported purposefully adding or missing a pill 1 day or more in the past week were categorized as low adherence.