## Title

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## Authors

Bloomfield, GS
Yi, SS
Astor, BC
et al.

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# Blood pressure and chronic kidney disease progression in a multi-racial cohort: the Multi-Ethnic Study of Atherosclerosis

**GS Bloomfield**[1,2], **SS Yi**[3], **BC Astor**[3,4,5], **H Kramer**[6], **S Shea**[7,8], **MG Shlipak**[9,10], and **WS Post**[3,11]

[1]Division of Cardiology, School of Medicine, Duke University, Durham, NC, USA

[2]Duke Clinical Research Institute, Duke University, Durham, NC, USA

[3]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

[4]Welch Center for Prevention, Epidemiology and Clinical Research, Baltimore, MD, USA

[5]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

[6]Department of Preventive Medicine, Loyola Medical Center, Maywood, IL, USA

[7]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA

[8]Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, NY, USA

[9]Department of Medicine, University of California, San Francisco, San Francisco, CA, USA

[10]General Internal Medicine Section, San Francisco Veterans Affairs Medical Center, San Francisco, CA, USA

[11]Ciccarone Center for the Prevention of Heart Disease, Division of Cardiology, Department of Medicine, Johns Hopkins School of Medicine, Baltimore, MD, USA.

## Abstract

The relationship between blood pressure (BP) and kidney function among individuals with chronic kidney disease (CKD) remains controversial. This study evaluated the association between BP and estimated glomerular filtration rate (eGFR) decline among adults with nondiabetic stage 3 CKD. The Multi-Ethnic Study of Atherosclerosis participants with an eGFR 30–59 ml $min^{-1}$ per 1.73 $m^2$ at baseline without diabetes were included. Participants were followed over a 5-year period. Kidney function change was determined by annualizing the change in eGFR using cystatin C, creatinine and a combined equation. Risk factors for progression of CKD (defined as a decrease in annualized eGFR >2.5 ml $min^{-1}$ per 1.73 $m^2$) were identified using univariate analyses and sequential logistic regression models. There were 220 participants with stage 3 CKD at baseline using cystatin C, 483 participants using creatinine and 381 participants using the combined equation. The median (interquartile range) age of the sample was 74 (68–79) years. The incidence of progression of CKD was 16.8% using cystatin C and 8.9% using creatinine ($P = 0.002$). Systolic BP >140 mm Hg or diastolic BP >90 mm Hg was significantly associated with



Correspondence: Dr WS Post, Division of Cardiology, Department of Medicine, Johns Hopkins University, Carnegie 568, 600 North Wolfe Street, Baltimore, MD 21287, USA. wpost@jhmi.edu.

CONFLICT OF INTEREST
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progression using a cystatin C-based (odds ratio (OR), 2.49; 95% confidence interval (CI), 1.12–5.52) or the combined equation (OR, 2.07; 95% CI, 1.16–3.69), but not when using creatinine after adjustment for covariates. In conclusion, with the inclusion of cystatin C in the eGFR assessment hypertension was an important predictor of CKD progression in a multi-ethnic cohort with stage 3 CKD.

### Keywords

blood pressure; glomerular filtration rate; renal disease; cystatin C; creatinine; ethnicity

## INTRODUCTION

Chronic kidney disease (CKD) increases risk of cardiovascular death, all-cause mortality, cardiovascular events and hospitalization regardless of ethnicity or sex.[1–3] A large proportion of CKD in the United States is attributed to hypertension,[4] but the association between blood pressure (BP) and CKD progression remains unclear. Although some large randomized studies suggest that lowering BP in patients with CKD has no effect on the rate of glomerular filtration rate (GFR) decline,[5,6] observational studies and per-protocol analyses have shown a protective effect of tight BP control in patients across many stages of CKD.[7–9] Despite disparate findings from large studies, adequate BP control is still widely considered an important intervention for slowing loss of GFR among individuals with CKD.[10,11] This is especially important for individuals with stage 3 CKD, who have a high rate of GFR decline[8,12] and represent the majority of individuals with CKD.[13] The method of GFR estimation is also important, as the mortality risk is higher across all levels of decreased estimated GFR (eGFR) with cystatin C-based equations compared with creatinine-based equations.[14]

Previous studies addressing BP and CKD progression have been limited to adults with established CKD and do not include Asian or Hispanic race/ethnicity groups. The Multi-Ethnic Study of Atherosclerosis (MESA) represents a unique opportunity to explore the association between BP and CKD progression in a diverse group of adults, and previous analyses addressing kidney decline in MESA have been restricted to persons without baseline CKD.[15] The primary hypothesis of this study was that BP is inversely associated with rapid eGFR decline among participants with stage 3 CKD.

## PATIENTS AND METHODS

### Study participants

MESA was designed to study the prevalence, risk factors and progression of subclinical cardiovascular disease in a multi-ethnic cohort. A detailed description of the study design and methods has been published previously[16] and are available online at www.mesa-nhlbi.org. Briefly, 6814 participants, 45 to 84 years of age, who identified themselves as non-Hispanic white, African American, Hispanic or Chinese were recruited from six US communities during the years 2000–2002. All participants were free of clinically apparent cardiovascular disease. The communities included the following: Forsyth County, NC; Northern Manhattan and the Bronx, NY; Baltimore City and Baltimore County, MD; St Paul, MN; Chicago, IL; and Los Angeles County, CA. The Institutional Review Boards at all participating sites approved the study, and all participants gave informed consent. For the present analysis, we excluded participants with prevalent diabetes mellitus (fasting glucose $\geq 126 \quad \mathrm{mg} \quad \mathrm{dl}^{-1}$ or use of diabetes medications), because of the strong association between diabetes, hypertension and CKD. We included only those participants who had

serum creatinine or cystatin C, and BP measured at baseline (2000–2002), and at Exam 3 (2004–2005) or Exam 4 (2005–2007); participants missing data owing to dropout or death were not included in this analysis. Stage 3 CKD was defined according to the National Kidney Foundation and the Kidney Disease Outcomes Quality Initiative definitions (that is, eGFR 30–59 ml $min^{-1}$ per 1.73 $m^2$).[17]

### Definitions of progression of kidney disease

Exams occurred approximately every 1.5 years, and serum creatinine and cystatin C were measured at examinations 1, 3 and 4. Serum creatinine was measured by rate reflectance spectrophotometry using thin-film adaptation of the creatinine amidinohydrolase method on the Vitros analyzer (Johnson & Johnson Clinical Diagnostics, Rochester, NY, USA). Creatinine measurements were indirectly calibrated to the isotope dilution mass spectrometry-traceable CX3 method: recalibrated serum creatinine = 0.9954 × measured serum creatinine – 0.0208. Serum cystatin C was measured using a BNII Nephelometer (Dade Behring, Deerfield, IL, USA), which uses a particle-enhanced immunepholometric assay (N Latex Cystatin C) on fasting samples stored at –70 °C. The assay is stable over five cycles of freeze/thaw. GFR was estimated using the following formulae using serum cystatin C (estimated GFR using cystation C (eGFRcys)), creatinine (estimated GFR using creatinine (eGFRcreat)) and a combined equation (estimated GFR using cystation C and creatinine (eGFRcomb)):

> eGFRcys in ml $min^{-1}$ per 1.73 $m^2$ = 127.7 × (cystatin C)$^{-1.17}$ × (Age)$^{-0.13}$ × (0.91 if female) × 1.06 (if African American)[18]
>
> eGFRcreat in ml $min^{-1}$ per 1.73 $m^2$ = 186 × (recalibrated serum creatinine)$^{-1.154}$ × (Age)$^{-0.203}$ × (0.742 if female) × (1.210 if American)[19]
>
> eGFRcomb in ml $min^{-1}$ per 1.73 $m^2$ = 135 × min (recalibrated serum creatinine/$\kappa$, 1)$^{\alpha}$ × max (recalibrated serum creatinine/$\kappa$, 1)$^{-0.601}$ × min (cystatin C/0.8, 1)$^{-0.375}$ × max (cystatin C/0.8, 1)$^{-0.711}$ × $0.995^{Age}$ (× 0.969 if female) (× 1.08 if black), where $\kappa$ is 0.7 for females and 0.9 for males, $\alpha$ is –0.248 for females and –0.207 for males, min indicates the minimum of creatinine/$\kappa$ or 1, and max indicates the maximum of creatinine/$\kappa$ or 1[20]

Baseline clinical and renal function characteristics of the entire MESA cohort were published in 2008.[21] Using eGFRcys, there were 275 nondiabetic participants with stage 3 CKD at baseline (prevalence = 4.0%). Fifty-five participants were missing data on cystatin C at Exam 3 and 4, and were not included in the analysis. Among the remaining 220 participants with CKD stage 3 by cystatin C, 169 had cystatin C measures for examinations 1, 3 and 4; 37 for examinations 1 and 3; and 14 for examinations 1 and 4. There were 544 nondiabetic participants with stage 3 CKD at Exam 1 using eGFRcreat (prevalence = 8.0%). Sixty-one of these participants were missing data on creatinine at Exam 3 and 4, and are therefore not included in the analyses. Among the remaining 483 participants with stage 3 CKD by eGFRcreat at the baseline examination, 431 had creatinine available at Examinations 1, 3 and 4; 41 had creatinine available only at Examinations 1 and 3; and 11 had creatinine available only at Examinations 1 and 4.

The slope of eGFR change was calculated between visit dates for each individual and then annualized. Previous research has suggested an eGFR decline of more than 3 ml $min^{-1}$ per 1.73 $m^2$ identifies persons who have rapid decline in eGFR.[22,23] Because of the small number of progressors identified in this analysis when 3 ml $min^{-1}$ per 1.73 $m^2$ was used, we defined progressors as those participants whose eGFR declined by more than 2.5 ml $min^{-1}$ per 1.73 $m^2$ per year. Nonprogressors were defined as those participants whose eGFR increased or declined by less than or equal to 2.5 ml $min^{-1}$ per 1.73 $m^2$ per year.

### Blood pressure

Trained and certified clinic staff obtained BP and anthropometric measurements on all MESA participants during the baseline visit. BP was measured three times at 1-min intervals, using a Dinamap PRO 100 (General Electric Medical Systems, Milwaukee, WI, USA) automated oscillometric device. The average of the second and third measurements was used for this analysis. Systolic BP (SBP) was divided into three categories as follows: <130 mm Hg, $\geq 130 \quad \mathrm{mm} \quad \mathrm{Hg}$ to <140 mm Hg and $\geq 140 \quad \mathrm{mm} \quad \mathrm{Hg}$. Diastolic BP (DBP) was divided into: <80 mm Hg, $\geq 80 \quad \mathrm{mm} \quad \mathrm{Hg}$ to <90 and $\geq 90 \quad \mathrm{mm} \quad \mathrm{Hg}$. Hypertension was defined as SBP >140 mm Hg, DBP >90 mm Hg and/or use of anti-hypertensive medication.

### Covariates

All MESA subjects completed self-administered questionnaires and were interviewed by trained research staff, to collect information pertaining to demographic characteristics, medical history, medication, alcohol and tobacco use. These self-administered questionnaires were available in English, Spanish and Chinese. Urine albumin and creatinine were measured on a single-spot sample using nephelometry. The presence of any albuminuria was defined as a spot urine albumin/creatinine ratio >30 mg $g^{-1}$. Albumin/creatinine ratios were log-transformed for analysis. Height was measured to the nearest 0.1 cm with the subject in stocking feet, and weight was measured to the nearest pound with the subject in light clothing using a balanced scale. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured at the umbilicus to the nearest 0.1 cm using a steel measuring tape with standard 4 oz tension.

### Statistical analyses

Baseline characteristics were compared by CKD progression status using Student's *t*-tests and $\chi^2$-tests for continuous and dichotomous variables. Non-parametric tests were used for variables without a normal distribution. Multivariable logistic regression was used to examine the association between BP and eGFR progression. Separate analyses were conducted with eGFR progression defined using eGFRcys, eGFRcreat and eGFRcomb. Several models were constructed to examine the association between BP and CKD progression, using the three equations for eGFR. We first developed a baseline set of covariates including age, sex, race/ethnicity, BMI and albuminuria. To this base model, we added the following BP-related covariates individually: SBP $\geq 130 \quad \mathrm{mm} \quad \mathrm{Hg}$; SBP as a continuous variable; SBP >140 mm Hg or DBP >90 mm Hg; use of anti-hypertensive medications; and hypertension (SBP >140 mm Hg, DBP >90 mm Hg and/or use of anti-hypertensive medication). Similar models were generated after replacing BMI with waist circumference or body surface area. Odds ratios (OR) are reported with 95% confidence intervals.

## RESULTS

### Prevalence of stage 3 CKD

The prevalence of stage 3 CKD using eGFRcys for each racial/ethnic group were: white 4.3% (113/2 620), Chinese 1.7% (14/802), black 2.8% (53/1 892) and Hispanic 2.7% (40/1 496). The prevalence of stage 3 CKD using eGFRcreat for each racial/ethnic group were: white 12.0% (314/2 620), Chinese 7.7% (62/802), black 4.7% (89/1 892) and Hispanic 5.3% (79/1 496). The overall prevalences of stage 3 CKD at the baseline exam calculated using eGFRcys and eGFRcreat were 4.0% and 8.0%, respectively.

There were 37 progressors (16.8% incidence) and 183 nonprogressors during follow-up using eGFRcys (Table 1). There were no differences between racial/ethnic groups between progressors and nonprogressors, and baseline serum cystatin C levels were similar in both groups. In unadjusted analyses, progressors were more likely to have an SBP >140 mm Hg or DBP >90 mm Hg than nonprogressors (54% vs 32%, $P = 0.01$) and to be on anti-hypertensive medication (83% vs 59%, $P = 0.006$). Greater than 50% of progressors had albuminuria at baseline, whereas only 16% of nonprogressors had albuminuria ($P<0.001$).

Using eGFRcreat, there were 43 progressors (8.9% incidence) and 440 nonprogressors during follow-up (Table 2). The incidence of eGFR loss >2.5 ml $min^{-1}$ per 1.73 $m^2$ was significantly higher using a cystatin C-based equation than using a creatinine-based equation (16.8% vs 8.9%, $P = 0.002$). In unadjusted analyses, progressors were older than nonprogressors (72 vs 68 years, $P<0.001$), and blacks and Hispanics were disproportionately represented. Progressors were more likely to have a SBP >130 mm Hg at baseline, and to be hypertensive compared with nonprogressors. The average baseline SBP but not DBP was higher among progressors compared with nonprogressors. Baseline eGFRcreat was slightly lower and creatinine was higher among progressors. A higher proportion of progressors (40%) than nonprogressors (24%) were taking angiotensin-converting enzyme inhibitor or angiotensin receptor blocker medications ($P = 0.03$). There were no other significant differences in medication usage patterns. A greater proportion of progressors had albuminuria than the nonprogressors (28% vs 13%, $P = 0.005$).

Using the combined equation for eGFR, there were 65 progressors and 316 nonprogressors yielding an incidence of progression of 17% (Table 3). Most of the progressors were men. Similar to the results of the cystatin C- and creatinine-based equations, progressors were more likely to have higher BP than nonprogressors, and to be on a greater number of anti-hypertensive medications.

Table 4 shows the sequential logistic regression models performed to describe the relationship between the covariates and progression of CKD using eGFRcys, eGFRcreat and eGFRcomb. There were no significant relationships between race/ethnicity and CKD progression using eGFRcys. Using eGFRcys, SBP >140 mm Hg or DBP >90 mm Hg strongly predicted progression (OR, 2.49; 95% CI, 1.12–5.52) as did being on anti-hypertensive medication (OR, 3.46; 95% CI, 1.30–9.25) and the definition of hypertension (OR, 5.10; 95% CI, 1.42–18.35). Using eGFRcreat, there was no statistically significant relationship between higher BP and progression of CKD, and only SBP >140 mm Hg or DBP >90 mm Hg was marginally associated (OR, 1.78; 95% CI, 0.91–3.52). In all of the models using eGFRcreat, black and Hispanic race/ethnicity were strongly and significantly associated with progression. Using the combined equation, the results were most similar to the models using eGFRcys in that measures of high BP were the strongest predictors of progression. The only racial/ethnic difference found using eGFRcomb was a lower risk of progression among the Chinese group. There were no significant changes in the results when socio-economic status variables or individual MESA field center were included in the models. Removing race from the models in Table 3 or replacing waist circumference or body surface area for BMI did not significantly alter the BP association results (data not shown). Similarly, there were no apparent differences when the models were stratified for median BMI or waist circumference.

## DISCUSSION

The relationship between BP and progression of nondiabetic kidney disease has been the subject of debate for many years. In the present analysis, we have made several observations. First, we found that when we used eGFRcys, each hypertension definition was

strongly and independently associated with progression. Using eGFRcreat, higher SBP was associated with progression of stage 3 CKD in unadjusted analyses; however, after covariate adjustment, the association between BP level and progression was weaker. Using the combined cystatin C and creatinine equation (CKD-Epidemiology Collaboration combined equation), we found that hypertension was strongly associated with progression, similar to the results when using eGFRcys. Second, race/ethnicity was not associated with CKD progression using eGFRcys, but black and Hispanic race/ethnicity were associated with progression of CKD using eGFRcreat.

Large, prospective randomized studies and retrospective analyses have shown conflicting findings regarding the association of BP level and progression of nondiabetic CKD. The African American Study of Kidney Disease and Hypertension randomized 1094 African Americans with hypertensive renal disease (GFR between 20 and 65 ml $min^{-1}$ per 1.73 $m^2$) to intensive BP control or usual care.[5] Participants randomized to intensive BP control had the same rate of GFR decline over 4 years as participants in the usual care arm of the study. Ten year follow-up data in the cohort phase of the African American Study of Kidney Disease and Hypertension also showed similar findings in terms of kidney disease progression, but also demonstrated modification of the effect of BP control by the presence of albuminuria with the greatest benefit from lower BP occurring in those with albuminuria.[24] The Modification of Diet in Renal Disease Study Group compared two groups of participants with nondiabetic kidney disease randomized to usual BP control or more aggressive control over a 3-year period.[25] Aggressive BP control showed no or modest benefit in those with less than 3 g per day of proteinuria, but a clinically and statistically significant slowing of the rate of progression with aggressive BP control in those with >3 g per day of proteinuria. Subgroup analysis of the long-term outcomes of patients enrolled in the initial Modification of Diet in Renal Disease study showed that the benefit of more aggressive BP control was limited to patients with significant protein excretion.[8] The Ramipril Efficacy in Nephropathy-2 trial also showed no significant protection from progression of CKD with intensive BP control in patients with nondiabetic kidney disease, despite a significant decrease in SBP.[26] In contrast to the current analysis, in these studies, GFR was either measured using $^{125}$I-iothalamate or estimated using creatinine-based equations. Moreover, the mean eGFR in the African American Study of Kidney Disease and Hypertension was slightly lower (45 ml $min^{-1}$ per 1.73 $m^2$)[5] than in our analysis (52 ml $min^{-1}$ per 1.73 $m^2$), and interventions at this stage may have a smaller effect on the BP–CKD progression relationship.

Using eGFRcys and eGFRcomb, we found that SBP $\geq 130 \quad \mathrm{mm} \quad \mathrm{Hg}$ was associated with progression of CKD in univariate analyses. Moreover, in our multivariable analyses, the odds of an individual with stage 3 CKD progressing was five times greater in those with hypertension (SBP >140 mm Hg, DBP >90 mm Hg or on treatment) compared with those without hypertension. This relationship persisted if we used the BP cut-off values (OR, 2.49; 95% CI, 1.12–5.52) or use of anti-hypertensive medications classification (OR, 5.10; 95% CI, 1.42–18.35), and after adjustment for BMI, waist circumference and albuminuria. However, the relationship between BP and progression was contingent upon the method used to estimate GFR, as these associations were not seen when creatinine-based equations were utilized. Serum cystatin C is a nonglycosylated basic protein produced at a constant rate by all nucleated cells. It is freely filtered by the renal glomeruli and primarily catabolized in the proximal tubule. Serum cystatin C concentration is slightly (~12%) higher in males compared with females, and is generally lower among non-Hispanic black and Mexican Americans compared with non-Hispanic white Americans.[27] In contrast, creatinine is a byproduct of muscle breakdown and, as such, circulating levels are affected by an individual's muscle mass.[28] Although serum cystatin C levels may also be affected by other clinical factors,[29] it is generally considered a better measure of GFR than serum creatinine

with greater accuracy, sensitivity and similar specificity.[30,31] It is possible that difference in test characteristics contributed to the differences in this analysis. However, in the absence of an actual measured GFR, it is beyond the scope of this analysis to determine which assay provides the best estimate of GFR. Our analyses suggest that it may be worthwhile to explore the BP–CKD progression in future studies by using and combining both assays and a measured GFR, to better understand the appropriate use of each measure.

Guidelines for the management of high BP, and many clinicians, have advocated for lower BP goals for patients with CKD.[11] This opinion, however, has been called into question, as these guidelines have been almost exclusively based on observational data rather than prospective, randomized clinical trials. The conflicting opinions may be related to a number of factors, including the short length of follow-up relative to the slow progression of CKD, the assay used to estimate GFR and the presence of albuminuria. Although it may take decades for the effects of BP to manifest as CKD progression, few studies have had follow-up greater than 10 years.[32] Also, albuminuria is thought to be both a marker of CKD severity and also a mediator of the effect of SBP on CKD progression. In our analysis, albuminuria was an independent predictor of CKD progression and remained strongly associated with CKD progression in multivariable models using either assay. This finding is consistent with prior studies that have demonstrated that the presence of albuminuria is a main factor that determines whether lower BP prevents progression of renal disease.[24,25]

Several limitations should be acknowledged. We did not have follow-up serum creatinine and cystatin C available for all participants with stage 3 CKD. Participants who were missing these data tended to be older and have higher BP. We may have slightly underestimated the rate of progression of CKD, as we would expect a higher BP among progressors. However, we had follow-up data available on approximately 90% of participants with stage 3 CKD at baseline, and our findings are unlikely to have been substantially different if we had complete follow-up data. Second, our analysis is limited by the relatively small number of participants with stage 3 CKD by eGFRcys. A strength, however, is that this study is population-based, unlike many other studies, which focused on patients with known CKD. Finally, three estimates of GFR were used in this analysis, including a combined equation,[20] which provided a more comprehensive approach; however, we did not have directly measured GFR.

In conclusion, estimates of GFR that include cystatin C demonstrate that hypertension is an important predictor of progression of stage 3 CKD in a multi-ethnic cohort and do not demonstrate the same racial/ethnic differences suggested by creatinine-based estimates. The impact of type of assay used to estimate GFR in diverse populations should be explored and compared with directly measured GFR.

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*What is known about this topic:*

- High BP is a leading cause of CKD. High BP is a major cause of CKD among various racial/ethnic groups. Lowering BP is felt to be an important intervention to limit progression of CKD.
- The effect of high BP control on progression of CKD remains controversial. Large, randomized studies suggest that lowering BP in patients with CKD has no significant effect on GFR decline. In contrast, observational studies show a protective effect of tight BP control.
- Estimates of GFR vary depending on the assay used. Creatinine levels are influenced by muscle mass and GFR levels may differ between individuals for a given serum creatinine. Estimates of GFR using cystatin C may be more similar across racial/ethnic groups compared with estimates using creatinine.

*What this study adds:*

- In a multi-racial cohort, higher BP predicts progression of CKD. In analyses using cystatin C, higher BP is strongly and independently associated with progression of stage 3 CKD. The effect of BP on the progression of CKD was similar among white, black, Hispanic and Chinese participants in the MESA when cystatin C was used to eGFR.
- Cystatin C-based estimates of GFR do not demonstrate the same racial/ethnic differences suggested by creatinine. Racial/ethnic group attenuated the relationship between BP and progression of CKD when creatinine was used to estimate the GFR. Racial/ethnic group significantly predicted the progression of CKD, and the effect of BP was attenuated when creatinine was used.

## Table 1

Univariate baseline risk factors for progression during follow-up using cystatin C-based GFR ($n = 220$)[a]

| *Risk factor* | *Progressors (n = 37)* | *Nonprogressors (n = 183)* | P-*value* |
|---|---|---|---|
| Age (years) | 71 (9) | 70 (10) | 0.38 |
| Female (%) | 32 | 46 | 0.12 |
| *Ethnicity (%)* | | | |
| White | 54 | 51 | |
| Chinese | 5 | 7 | |
| Black | 22 | 25 | |
| Hispanic | 19 | 18 | 0.97 |
| *SBP categorical (%)* | | | |
| < 130 mm Hg | 38 | 49 | |
| 130–139 mm Hg | 11 | 19 | |
| ≥ 140 mm Hg | 51 | 32 | 0.07 |
| *SBP binary (%)* | | | |
| < 130 mm Hg | 38 | 49 | |
| ≥ 130 mm Hg | 62 | 51 | 0.21 |
| *DBP categorical (%)* | | | |
| < 80 mm Hg | 73 | 81 | |
| 80–89 mm Hg | 22 | 14 | |
| ≥ 90 mm Hg | 5 | 5 | 0.51 |
| SBP (mm Hg) | 139 (22) | 132 (22) | 0.08 |
| DBP (mm Hg) | 72 (11) | 71 (11) | 0.60 |
| SBP > 140 mm Hg or DBP > 90 mm Hg (%) | 54 | 32 | 0.01 |
| On BP medications (%) | 83 | 59 | 0.006 |
| SBP > 140 mm Hg or DBP > 90 mm Hg or on BP medications (%) | 92 | 67 | 0.003 |
| Albuminuria (%) | 51 | 16 | < 0.001 |
| eGFRcys at Exam 1 (ml $min^{-1}$ per 1.73 $m^2$) | 51 (7) | 53 (7) | 0.25 |
| Cystatin C at Exam 1 (mg $l^{-1}$) | 1.4 (0.2) | 1.4 (0.2) | 0.25 |
| *Number of BP medications (%)* | | | |
| None | 28 | 49 | |
| One | 42 | 32 | |
| Two | 19 | 17 | |
| Three | 11 | 2 | 0.01 |
| On an ACEi or ARB (%) | 36 | 23 | 0.10 |
| On a CCB (%) | 39 | 16 | 0.001 |
| On a diuretic (%) | 39 | 33 | 0.52 |

Abbreviations: SBP, systolic BP; DBP, diastolic BP; GFR, glomerular filtration rate; BP, blood pressure; eGFRcys, estimated GFR using cystatin C; ACEi angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

[a]Mean values ± s.d. or % distribution. No differences were found between progressors and nonprogressors for current or recent financial strain, income or education, and these variables are not included in this table.

## Table 2

Univariate baseline risk factors for progression during follow-up using creatinine-based GFR ($n$ = 483)[a]

| *Risk factor* | *Progressors* (n = *43*) | *Nonprogressors* (n = *440*) | P-*value* |
|---|---|---|---|
| Age (years) | 72 (7) | 68 (9) | 0.002 |
| Female (%) | 51 | 62 | 0.17 |
| *Ethnicity (%)* | | | |
| White | 37 | 62 | |
| Chinese | 7 | 11 | |
| Black | 33 | 14 | |
| Hispanic | 23 | 14 | < 0.001 |
| *SBP categorical (%)* | | | |
| < 130 mm Hg | 33 | 48 | |
| 130–139 mm Hg | 12 | 18 | |
| ≥ 140 mm Hg | 56 | 33 | 0.01 |
| *SBP binary (%)* | | | |
| < 130 mm Hg | 33 | 48 | |
| ≥ 130 mm Hg | 67 | 52 | 0.05 |
| *DBP categorical (%)* | | | |
| < 80 mm Hg | 79 | 81 | |
| 80–89 mm Hg | 21 | 15 | |
| ≥ 90 mm Hg | 0 | 4 | 0.028 |
| SBP (mm Hg) | 142 (24) | 131 (21) | < 0.001 |
| DBP (mm Hg) | 72 (10) | 71 (10) | 0.48 |
| SBP > 140 mm Hg or DBP > 90 mm Hg (%) | 56 | 33 | 0.003 |
| On BP medications | 65 | 52 | 0.09 |
| SBP > 140 mm Hg or DBP > 90 mm Hg or on BP medications | 81 | 64 | 0.02 |
| Albuminuria (%) | 28 | 13 | 0.005 |
| eGFRcreat at Exam 1 (ml $min^{-1}$ per 1.73 $m^2$) | 51 (7) | 53 (6) | 0.05 |
| Creatinine at Exam 1 (mg $dl^{-1}$) | 1.4 (0.3) | 1.3 (0.2) | 0.03 |
| *Number of BP medications (%)* | | | |
| None | 44 | 54 | |
| One | 37 | 29 | |
| Two | 12 | 15 | |
| Three | 7 | 2 | 0.17 |
| On an ACEi or ARB (%) | 40 | 24 | 0.03 |
| On a CCB (%) | 16 | 15 | 0.86 |
| On a diuretic (%) | 26 | 26 | 0.98 |

Abbreviations: SBP, systolic BP; DBP, diastolic BP; GFR, glomerular filtration rate; BP, blood pressure; eGFRcreat, estimated GFR using creatinine; ACEi angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

[a]Mean values ± s.d. or % distribution. No differences were found between progressors and nonprogressors for current or recent financial strain, income or education, and these variables are not included in this table.

## Table 3

Univariate baseline risk factors for progression during follow-up using the combined cystatin C and creatinine-based GFR (n = 381)[a]

| *Risk factor* | *Progressors (n = 65)* | *Nonprogressors (n = 316)* | P-*value* |
|---|---|---|---|
| Age (years) | 73 (7) | 71 (9) | 0.14 |
| Female (%) | 43 | 60 | 0.01 |
| *Ethnicity (%)* | | | |
| White | 49 | 54 | |
| Chinese | 2 | 11 | |
| Black | 26 | 20 | |
| Hispanic | 23 | 15 | 0.03 |
| *SBP categorical (%)* | | | |
| < 130 mm Hg | 26 | 44 | |
| 130–139 mm Hg | 22 | 20 | |
| ≥ 140 mm Hg | 52 | 36 | 0.02 |
| *SBP binary (%)* | | | |
| < 130 mm Hg | 26 | 44 | |
| ≥ 130 mm Hg | 74 | 56 | 0.01 |
| *DBP categorical (%)* | | | |
| < 80 mm Hg | 75 | 83 | |
| 80–89 mm Hg | 22 | 13 | |
| ≥ 90 mm Hg | 3 | 4 | 0.20 |
| SBP (mm Hg) | 142 (22) | 134 (22) | 0.01 |
| DBP (mm Hg) | 73 (10) | 71 (10) | 0.14 |
| SBP > 140 mm Hg or DBP > 90 mm Hg (%) | 54 | 36 | 0.01 |
| On BP medications | 77 | 60 | 0.01 |
| SBP > 140 mm Hg or DBP > 90 mm Hg or on BP medications | 89 | 70 | < 0.01 |
| Albuminuria (%) | 31 | 15 | < 0.01 |
| eGFRcomb at Exam 1 (ml $min^{-1}$ per 1.73 $m^2$) | 53 (7) | 52 (7) | 0.66 |
| *Number of BP medications (%)* | | | |
| None | 31 | 47 | |
| One | 40 | 34 | |
| Two | 22 | 16 | |
| Three | 8 | 3 | 0.04 |
| On an ACEi or ARB (%) | 42 | 28 | 0.03 |
| On a CCB (%) | 28 | 16 | 0.03 |
| On a diuretic (%) | 37 | 30 | 0.28 |

Abbreviations: SBP, systolic BP; DBP, diastolic BP; GFR, glomerular filtration rate; BP, blood pressure; eGFRcomb, estimated GFR with combined equation using cystatin C and creatinine; ACEi angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

[a]Mean values ± s.d. or % distribution. No differences were found etween progressors and nonprogressors for current or recent financial strain, income or education, and these variables are not included in this table.

## Table 4

Sequential logistic regression analysis models for progression of CKD using cystatin C-, creatinine-based or combined cystatin C-creatinine eGFR

| Covariates | Cystatin C model[a] OR (95% CI) | Creatinine model[a] OR (95% CI) | Combined model[a] OR (95% CI) |
|---|---|---|---|
| *Race/ethnicity* | | | |
| White (reference group) | 1.00 | 1.00 | 1.00 |
| Chinese | 0.50 (0.95–2.61) | 0.85 (0.23–3.15) | **0.10 (0.01–0.81)** |
| Black | 0.68 (0.26–1.77) | **3.05 (1.32–7.00)** | 1.47 (0.73–2.95) |
| Hispanic | 0.73 (0.26–2.06) | **2.50 (1.04–6.02)** | 1.85 (0.90–3.82) |
| Age | 1.02 (0.98–1.06) | **1.06 (1.02–1.11)** | 1.02 (0.99–1.06) |
| Female | 0.70 (0.31–1.54) | 0.81 (0.41–1.62) | **0.47 (0.26–0.84)** |
| Body mass index | 0.99 (0.92–1.06) | 1.01 (0.94–1.09) | 0.98 (0.92–1.04) |
| Albuminuria | **1.51 (1.20–1.91)** | **1.32 (1.05–1.65)** | 1.20 (0.98–1.46)[c] |
| SBP binary[b] ≥ 130 mm Hg vs not | 1.40 (0.64–3.10) | 1.15 (0.56–2.37) | **2.29 (1.20–4.37)** |
| SBP (continuous) | 1.01 (1.00–1.03) | 1.01 (0.99–1.03) | **1.02 (1.00–1.03)** |
| SBP > 140 mm Hg or DBP > 90 mm Hg | **2.49 (1.12–5.52)** | 1.78 (0.91–3.52)[c] | **2.07 (1.16–3.69)** |
| On hypertension medications | **3.46 (1.30–9.25)** | 1.17 (0.58–2.36) | **2.50 (1.28–4.90)** |
| SBP > 140 mm Hg or DBP > 90 mm Hg or hypertension medications | **5.10 (1.42–18.35)** | 1.44 (0.62–3.35) | **4.24 (1.71–10.52)** |

Abbreviations: OR, odds ratio; CI, confidence interval; BP, blood pressure; SBP, systolic BP; DBP, diastolic BP; CKD, chronic kidney disease; GFR, glomerular filtration rate. Bold indicates significance $P < 0.05$.

[a]The ORs for the baseline set of covariates (race/ethnicity, age, sex, body mass index, albuminuria) in each column represent the unadjusted statistic. ORs for the baseline set of covariates were not significantly changed with the addition of BP-related variables.

[b]The four BP-related variables were added independently of each other to the baseline set of covariates.

[c]$P < 0.10$.