VALIDATION OF AN ALBUMINURIA SELF-ASSESSMENT TOOL IN THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS (MESA)

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Objective: We previously developed an 8-item self-assessment tool to identify individuals with a high probability of having albuminuria. This tool was developed and externally validated among non-Hispanic Whites and non-Hispanic Blacks. We sought to validate it in a multi-ethnic cohort that also included Hispanics and Chinese Americans.

Design: This is a cross-sectional study.

Setting: Data were collected using standardized questionnaires and spot urine samples at a baseline examination in 2000-2002. The 8 items in the self-assessment tool include age, race, gender, current cigarette smoking, history of diabetes, hypertension, or stroke, and self-rated health.

Participants: Of 6,814 community-dwelling adults aged 45-84 years participating in the Multi-Ethnic Study of Atherosclerosis (MESA), 6,542 were included in the primary analysis.

Main Outcome Measures: Albuminuria was defined as urine albumin-to-creatinine ratio ≥30 mg/g at baseline.

Results: Among non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and Chinese Americans, the prevalence of albuminuria was 6.0%, 11.3%, 11.6%, and 10.8%, respectively. The c-statistic for discriminating participants with and without albuminuria was .731 (95% CI: .692, .771), .728 (95% CI: .687, .761), .747 (95% CI: .709, .784), and .761 (95% CI: .699, .814) for non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and Chinese Americans, respectively. The self-assessment tool over-estimated the probability of albuminuria for non-Hispanic Whites and Blacks, but was well-calibrated for Hispanics and Chinese Americans.

Conclusions: The albuminuria self-assessment tool maintained good test characteristics in this large multi-ethnic cohort, suggesting it may be helpful for increasing awareness of albuminuria in an ethnically diverse population. Ethn Dis. 2015;25(4):427-434; doi:10.18865/ed.25.4.427

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tool’s development and validation. Validation of the albuminuria self-assessment tool among Hispanic and Asian adults is necessary before it can be recommended for use in these populations. Therefore, we sought to assess the test characteristics (sensitivity, specificity, and positive and negative predictive values), discrimination, and calibration of the albuminuria self-assessment tool in a multi-ethnic cohort that included Hispanics and Chinese Americans. We also assessed the characteristics of the self-assessment tool for men and women, separately. To do so, we analyzed data from the Multi-Ethnic Study of Atherosclerosis (MESA).

Methods

Study Population

Details of the MESA study design and recruitment have been published previously. In brief, between July 2000 and August 2002, 6,814 community-dwelling adults aged 45-84 years who were free of clinically apparent cardiovascular disease were enrolled in MESA. Participants from four race/ethnicity groups (non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and Chinese Americans) were recruited from six US communities: Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; Northern Manhattan and the Bronx, New York; and St. Paul, Minnesota. The MESA study was approved by the institutional review boards of all participating centers, and written informed consent was obtained from all participants, including consent to use the data for scientific purposes. Approval to conduct the current analysis was granted by the institutional review board at the University of Alabama at Birmingham.

Data Collection

MESA data for the primary analysis were collected through a screening/recruitment questionnaire and a baseline examination. Additional data for the secondary analysis were collected during a follow-up examination occurring approximately 18 months after baseline. The eight items in the self-assessment tool collected at baseline included age, sex (male or female), race-ethnicity (non-Hispanic Black, non-Hispanic White, Hispanic, or Chinese American), cigarette smoking (current vs former or never), self-reported history of diabetes, hypertension, or stroke, and self-rated health (excellent, very good, good, fair, or poor). Demographic information and data on tobacco use, hypertension, diabetes, and self-rated health were obtained using standardized questionnaires. Current cigarette smoking was defined as having smoked cigarettes in the last 30 days. Hypertension and diabetes were defined by self-report of a prior diagnosis by a doctor or health professional. Individuals with a history of cardiovascular disease at baseline were not enrolled in MESA.

Definition of Albuminuria and Persistent Albuminuria

Using spot urine samples collected at baseline and exam 2, urinary albumin concentration was determined by nephelometry using the Array 360 CE Protein Analyzer (Beckman Instruments, Inc). Urinary creatinine was measured by the Jaffé rate method using the Vitros 950IRC instrument (Johnson & Johnson Clinical Diagnostics Inc). For our primary analysis, albuminuria was defined as an albumin-to-creatinine ratio ≥30 mg/g at the baseline exam. In a secondary analysis, the outcome was persistent albuminuria, defined as having an albumin-to-creatinine ratio ≥30 mg/g at both the baseline exam and exam 2.

Statistical Analysis

Of the 6,814 MESA participants who attended the baseline exam, we excluded those without information on components of the self-
assessment tool (n=94) or urinary albumin or creatinine (n=38), or who self-reported a prior diagnosis of kidney disease (n=140), resulting in the inclusion of 6,542 participants for the primary analysis. Using the albuminuria self-assessment tool developed in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, each MESA participant was assigned a predicted probability of having albuminuria at baseline using the following equation: exp(X)/(1+exp(X)) where X = -5.1062 + .0318 * (age in years) + .000994 * (age in years – 65) + .3476 * (1 for non-Hispanic Blacks, 0 for other race-ethnicities) + .2515 * (1 for men, 0 for women) + .4383 * (1 for current smokers, 0 for nonsmokers) + .2615 * (1 if self-rated health is good) + .5043 * (1 if self-rated health is fair) + .4545 * (1 if self-rated health is poor) + .8515 * (1 for self-report of a diagnosis of diabetes, 0 for those not reporting diabetes) + .3536 * (1 for prior stroke, 0 for those without a prior stroke). As the development of the self-assessment tool did not include Hispanics and Chinese Americans, we included them in the “other race-ethnicities” group. All analyses were conducted overall and separately for each race-ethnicity group (non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and Chinese Americans).

Participant characteristics, including the eight components of the self-assessment tool, were calculated for individuals with and without albuminuria, separately. We calculated sensitivity, specificity, and positive and negative predictive values for albuminuria associated with a probability ≥10%, the previously published cut-point for identifying a high probability of albuminuria on the self-assessment tool. We then calculated the c-statistic for discriminating MESA participants with and without albuminuria associated with the probability of having albuminuria on the self-assessment tool. The c-statistic is a measure of how well a model discriminates between individuals with and without a condition (eg, albuminuria). For the current analysis, the c-statistic is the proportion of all pairwise comparisons of participants, one with albuminuria and one without albuminuria, for which the participant with albuminuria had a higher predicted probability on the self-assessment tool. We used a 1,000 iteration bias-corrected bootstrap to create 95% confidence intervals (CI) around the c-statistics. This approach involves resampling (with replacement) from the available data to create a large number of samples to approximate the distribution of the c-statistic. The c-statistics in this sample are ordered from lowest to highest and the 25th and 975th values are considered the boundary for the 95% CI around the c-statistic. To assess calibration of the self-assessment tool, the observed and predicted prevalence of albuminuria was calculated by quintile of predicted probability. Since some people with albuminuria do not have it on re-retesting, we con-

| Table 1. Baseline characteristics of MESA participants by race-ethnicity and albuminuria status |
|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
|                                            | Non-Hispanic White (n=2,538) | Non-Hispanic Black (n=1,819) | Hispanic (n=1,417) | Chinese-American (n=768) |
|                                            | No albuminuria | Albuminuria | No albuminuria | Albuminuria | No albuminuria | Albuminuria | No albuminuria | Albuminuria |
|                                            | (n=2,387)   | (n=151)  | (n=1,613)   | (n=206)   | (n=1,253)   | (n=164)   | (n=685)   | (n=83)   |
| Age in years, mean (SD)                    | 62.1 (10.2) | 68.8 (9.6) | 61.7 (10.0) | 65.9 (9.5) | 60.7 (10.1) | 65.9 (10.9) | 61.5 (10.2) | 68.3 (9.7) |
| Male, %                                    | 47.8     | 51.7     | 43.9     | 50.5     | 48.7     | 47.0     | 48.3     | 42.2     |
| Current smoker, %                          | 11.3     | 13.3     | 17.9     | 16.5     | 13.7     | 12.8     | 5.6      | 4.8      |
| Hypertension, %                            | 30.4     | 56.3     | 52.3     | 74.8     | 31.0     | 64.6     | 29.1     | 60.2     |
| Diabetes, %                                | 4.7      | 13.9     | 12.7     | 41.3     | 12.8     | 42.7     | 7.9      | 34.9     |
| History of stroke, %                       | 0.0      | 0.0      | 0.0      | 0.0      | 0.0      | 0.0      | 0.0      | 0.0      |
| Self-rated health, %                       | Excellent | 28.1     | 12.6     | 11.8     | 6.3      | 9.2      | 6.7      | 4.2      | 2.4      |
|                                            | Very good | 44.3     | 46.4     | 31.9     | 21.4     | 23.5     | 16.5     | 29.4     | 14.5     |
|                                            | Good      | 24.4     | 32.4     | 44.2     | 46.6     | 50.8     | 58.5     | 64.2     | 79.5     |
|                                            | Fair      | 3.1      | 8.6      | 11.4     | 23.3     | 15.3     | 14.6     | 2.2      | 3.6      |
|                                            | Poor      | .1       | 0.0      | .7       | 2.4      | 1.2      | 3.7      | 0.0      | 0.0      |

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duction a secondary analysis wherein we examined the discrimination and test characteristics of the screening tool for identifying persistent albuminuria. These analyses were limited to the 5,911 MESA participants who attended, and had valid albuminuria measures, at both baseline and exam 2. We also assessed the test characteristics (sensitivity, specificity, and positive and negative predictive values), discrimination and calibration of the self-assessment tool for men and women, separately. All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

Participant Characteristics

Among non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and Chinese Americans, the prevalence of albuminuria was 6.0%, 11.3%, 11.6%, and 10.8%, respectively. On average, participants with albuminuria were older than those without albuminuria (Table 1). Participants with albuminuria were also more likely to self-report a history of hypertension or diabetes. Individuals with vs without albuminuria were more likely to report fair or poor health.

Validation of the Self-assessment Tool by Race/ethnicity

Test characteristics for the self-assessment tool identifying MESA participants with albuminuria are shown by race/ethnicity in Table 2. In the overall population, the sensitivity, specificity, positive predictive value, and negative predictive value were .72 (95% CI: .68, .76), .59 (95% CI: .58, .61), .17 (95% CI: .15 ,.18), and .96 (95% CI: .95, .96), respectively. The c-statistic for discriminating participants with and without albuminuria was .743 (95% CI: .722, .763). The discrimination was higher for Chinese Americans (c-statistic .761; 95% CI: .699, .814) and Hispanics (c-statistic .747; 95% CI: .709, .784), compared with non-Hispanic Whites (c-statistic .731; 95% CI: .692, .771) and non-Hispanic Blacks (.728; 95% CI: .687, .761). The self-assessment tool over-estimated the probability of albuminuria for non-Hispanic Whites and Blacks, but was well-calibrated for Hispanics and Chinese Americans (Figure 1).

Validation of the Self-assessment Tool for Persistent Albuminuria

The prevalence of persistent albuminuria was 3.5%, 6.8%, 7.3%, and 6.4% among non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and Chinese Americans, re-
spective. The sensitivity, specificity, positive predictive value, and negative predictive value for persistent albuminuria associated with a predicted probability ≥10% were .72 (95% CI: .67, .77), .66 (95% CI: .65, .67), .11 (95% CI: .10, .12), and .98 (95% CI: .97, .98), respectively (supplemental data available from lead author). The c-statistic for discriminating participants with and without persistent albuminuria was .756 (95% CI: .727, .780). The discrimination was higher for Hispanics (c-statistic .774; 95% CI: .728, .816) and Chinese Americans (c-statistic .758; 95% CI: .675, .827), compared with non-Hispanic Whites (c-statistic .740; 95% CI: .682, .789) and Blacks (c-statistic .743; 95% CI: .687, .790). The self-assessment tool over-predicted persistent albuminuria for each race-ethnicity group (supplemental data available from lead author).

Validation of the Self-assessment Tool by Sex

The prevalence of albuminuria was 9.5% and 9.0% among men and women, respectively, while the prevalence of persistent albuminuria was 6.6% and 4.6% among men and women, respectively. The c-statistics for albuminuria were .763 (95% CI: .733, .787) and .730 (95% CI: .701, .759) among men and women, respectively (data not shown). The c-statistic for persistent albuminuria was .759 (95% CI: .717, .793) for men and .723 (95% CI: .683, .768) for women. For both men and women, the self-assessment tool was well-calibrated for albuminuria but over-estimated the probability of persistent albuminuria (supplemental data available from lead author).

**Discussion**

Using data from a large multi-ethnic cohort, we validated a self-assessment tool designed to identify individuals with a high probability of albuminuria in non-Hispanic Whites, non-Hispanic Blacks, Hispanics and Chinese Americans. Although the tool demonstrated only moderate sensitivity and specificity, it maintained good discrimination in each race-ethnicity. The self-assessment tool was well-calibrated in Hispanics and Chinese Americans. Although the tool over-predicted albuminuria for non-Hispanic Whites and non-Hispanic Blacks in our study, it was well-calibrated among Whites and Blacks in our prior validation study using National Health and Nutrition Examination Survey (NHANES) data. When evaluated in men and women, the self-assessment tool performed well in each group with good discrimination and calibration statistics. Therefore, this tool could be used to increase albuminuria awareness among individuals with a high risk.

The early stages of CKD are usually asymptomatic and thus, awareness is low both in the general population and in high-risk populations. In a prior analysis of MESA data, albuminuria was associated with higher mean end-diastolic left ventricular mass and coronary artery calcification scores. In other studies, albuminuria has been associated with an increased risk for CVD events, ESRD, and death. These data suggest that early albuminuria detection could provide an opportunity for risk reduction. In 2000, the National Kidney Foundation developed a free voluntary community-based kidney health screening program (Kidney Early Evaluation Program [KEEP]) to identify individuals at greatest risk of CKD, particularly those with diabetes or hypertension. Since its inception, KEEP has screened approximately 185,000 high-risk individuals. Although awareness of CKD is increasing, overall rates remain low.

While screening for albuminuria is feasible in a primary care setting, population-wide albuminuria screening is not recommended and studies show it is likely not cost-effective. However, data have suggested it is cost-effective to screen for albuminuria in high-risk populations. The American Diabetes Association recommends screening for CKD in all patients with diabetes and several organizations, including the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC), recommend screening patients being treated for hypertension. The self-assessment tool provides an opportunity to identify high-risk individuals for albuminuria screening.

The prevalence of albuminuria was higher among Hispanics and Chinese Americans compared with non-Hispanic Whites in our study, highlighting the importance of increasing awareness among these groups. Among Hispanics, a recent study of NHANES participants demonstrated a higher odds of albu-
minuria compared to Whites (multivariable adjusted odds ratio: 1.65; 95% CI: 1.07, 2.54). Furthermore, the incidence of ESRD among Hispanics in the United States is 1.8 times higher than that of Whites. Among Asians, data suggest that the risk of ESRD is similar to that of Whites. Hispanics, but not Asians, are also more likely to forego medical visits than Whites, particularly in the wake of the “Great Recession” of 2007-2009. As such, a self-assessment tool may be especially important for increasing awareness of CKD in Hispanics.

Framingham study data show that men have an increased risk for incident albuminuria compared to women (OR: 1.89; 95% CI: 1.37, 2.56). However, men are also less likely than women to utilize many health care services. In a cohort of 1,742 US adults participating in targeted, free, community-based CKD screenings, 70% were women. This suggests a potential unmet need for screening strategies for men at high risk for CKD. The self-assessment tool validated in our study demonstrated good discrimination and calibration for both men and women, suggesting it may be useful for increasing albuminuria awareness, particularly among men who otherwise would not utilize screening services.

The albuminuria self-assessment tool validated in our study includes eight items that are individually associated with albuminuria. In development of the self-assessment tool, the items in aggregate provided significantly better discrimination than any of the items individually. Although self-assessment tools such as the one validated in our study allow for widespread use, they do not provide clinical diagnoses. Individuals with a high probability for albuminuria based on the self-assessment tool should be recommended for further screening using spot urine testing for albuminuria. The best approach for effectively communicating the need for screening for individuals who test positive on the albuminuria self-assessment tool warrants further study. Also, the overall sensitivity and specificity were modest (72% and 59%, respectively) and future studies may identify screening tools with improved test characteristics.

Our study has a number of strengths. The albuminuria self-assessment tool validated in our study demonstrated good discrimination and calibration for both men and women, suggesting it may be useful for increasing albuminuria awareness, particularly among men who otherwise would not utilize screening services.

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In conclusion, albuminuria is an important risk factor for ESRD, CVD, and mortality. Early detection and treatment may reduce the risk of these events. However, despite the prognostic importance of albuminuria and the availability of effective treatments for it, awareness of albuminuria in the general population is low. In our study, we have externally validated an albuminuria self-assessment tool among non-Hispanic Whites, non-Hispanic Blacks,
Hispanics and Chinese Americans. The tool maintained good discrimination and calibration in this large multi-ethnic cohort, suggesting it may be helpful for increasing awareness of albuminuria in an ethnically diverse population.

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AUTHOR CONTRIBUTIONS

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