Original Investigation

Estimated Albumin Excretion Rate Versus Urine Albumin-Creatinine Ratio for the Assessment of Albuminuria: A Diagnostic Test Study From the Prevention of Renal and Vascular Endstage Disease (PREVEND) Study

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Background: Albumin-creatinine ratio (ACR) in spot urine samples is recommended for albuminuria screening instead of measured albumin excretion rate (mAER) in 24-hour urine collections. In patients with extremes of muscle mass, differences in spot urine creatinine values may lead to under- or overestimation of mAER by ACR. We hypothesized that calculating estimated AER (eAER) using spot ACR and estimated creatinine excretion rate (eCER) may improve albuminuria assessment.

Study Design: Diagnostic test study.

Setting & Participants: 2,711 community-living individuals from the general population of the Netherlands participating in the PREVEND (Prevention of Renal and Vascular Endstage Disease) Study.

Index Test: eAER was computed as the product of ACR and eCER. eCER was computed using 3 previously validated methods (Ix, Ellam, and Walser).

Reference Test: mAER, based on two 24-hour urine collections. Accuracy of the eAER and ACR were defined as the percentage of participants falling within 30% (P_{30}) of mAER.

Results: Mean age was 49 years, 46% were men, mean estimated glomerular filtration rate was 84 ± 15 mL/min/1.73 m^2, and median mAER was 7.2 (IQR, 5.4-11.0) mg/d. Mean measured CER was 1,381 mg/d, and median ACR was 4.9 mg/g. Using the Ix equation, median eAER was 6.4 mg/d. In the full cohort, eAER was more accurate and less biased compared to ACR (P_{30}, 48.9% vs 33.6%; bias, −34.2% vs −14.1%, respectively). In subgroup analysis, improvement was most notable in the middle and highest weight tertiles and in men. Using the other methods for eCER produced similar results.

Limitations: Little ethnic heterogeneity and a generally healthy cohort make extension of findings to other races and the chronically ill uncertain.

Conclusions: In a large community-dwelling cohort, eAER was more accurate than ACR in assessing albuminuria.

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INDEX WORDS: Albuminuria; albumin-creatinine ratio; creatinine excretion.

S pot (untimed) urinary protein or albumin-creatinine ratios (ACRs) from first morning void specimens have largely replaced timed urine collections for proteinuria screening in outpatient settings. Several studies suggest that spot ACR is a reasonably accurate indicator of albuminuria,[1,2] and KDIGO (Kidney Disease: Improving Global Outcomes) guidelines now consider ACR an acceptable first-line screening test.[3] ACR uses urine creatinine level in the denominator to correct for urine tonicity. However, creatinine excretion also is influenced by muscle mass, suggesting that ACR may be prone to bias introduced by differences in muscle mass.[4] We and others have shown that older age, female sex, and lower body weight are associated with higher ACR, independent of measured 24-hour urine albumin excretion, likely reflecting lower muscle mass in these groups, leading to lower urine creatinine excretion and thus higher ACR.[5,6]

We previously have developed and validated an equation that incorporates age, sex, race, and weight as proxies of muscle mass to calculate 24-hour estimated creatinine excretion rate (eCER).[7] In the

present study, we hypothesize that multiplying first morning void ACR by eCER to determine estimated albumin excretion rate (eAER) will attenuate the bias introduced by variable creatinine excretion between individuals, leading to a more accurate estimation of AER compared to spot first morning void ACR alone. To test this hypothesis, we examined the relationships of eAER and ACR with timed urine collections in 2,711 participants in the PREVEND (Prevention of Renal and Vascular Endstage Disease) Study and compared eAER with the performance of previously developed eCER equations.

METHODS

Participants

The PREVEND Study was designed to investigate the relationship of urinary albumin excretion with kidney and cardiovascular disease in a large cohort drawn from the general population of the city of Groningen, the Netherlands. Details of the protocol have been described elsewhere.[8,9] In brief, all inhabitants of the city of Groningen aged 28-75 years were sent a questionnaire and a vial to collect a first morning void urine sample. Urine albumin and creatinine were measured in the 40,856 (47.8%) who

responded ([Fig 1](#)). Participants with type 1 diabetes mellitus and pregnant women were excluded. All individuals with urinary albumin concentration ≥ 10 mg/L (n = 7,768) were invited to participate in PREVEND, and 6,000 consented and agreed. A randomly selected sample of individuals with urinary albumin concentration < 10 mg/L (n = 3,394) also was invited, and 2,592 agreed. The PREVEND cohort therefore constitutes 8,952 participants, who were asked to participate in a clinic visit that involved collecting 2 consecutive-day 24-hour urine samples. The PREVEND Study has been approved by the local ethics committee and was performed in accordance with Declaration of Helsinki guidelines.

For this analysis, all 2,592 participants with urine albumin excretion < 10 mg/L on the first morning void specimen were included. In addition, we included a computer-generated random sample of 828 individuals who had urine albumin concentrations ≥ 10 mg/L, leading to a total of 3,420 participants. This number of individuals was chosen to reconstitute a study sample with urine albumin concentrations representative of the 40,856 total respondents from Groningen. We excluded participants with missing spot urine albumin or creatinine data (n = 709). The remaining 2,711 participants comprised the study sample for this analysis.

All participants completed a questionnaire regarding health, demographic, and family history. Blood pressure measurements, anthropometric data (height and weight), and fasting venous blood
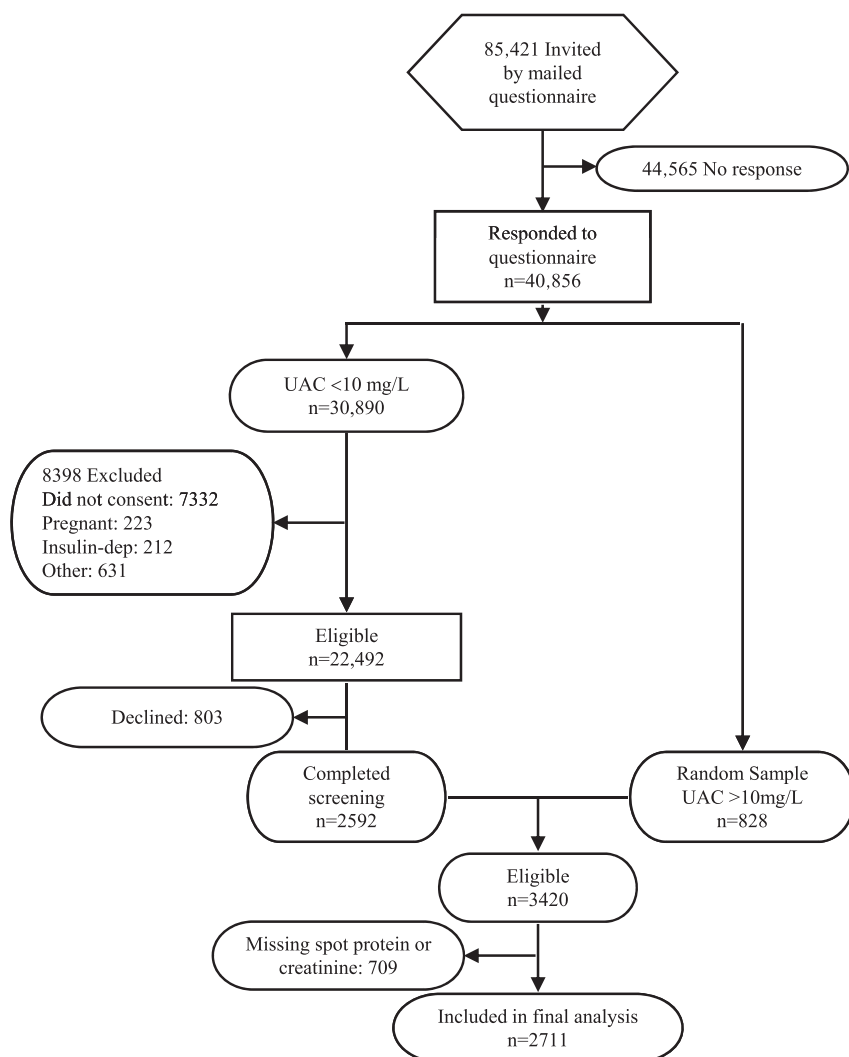
Figure 1. Participant selection for the PREVEND (Prevention of Renal and Vascular Endstage Disease) cohort. Abbreviations: dep, dependent; UAC, urine albumin creatinine.