Prevalence and complications of chronic kidney disease in a representative elderly population in Iceland

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ABSTRACT

Background. Chronic kidney disease (CKD) is common in the elderly, but data are limited on the distribution of glomerular filtration rate (GFR) and albuminuria and the prevalence of CKD and related complications in this population.

Methods. A cross-sectional study of 3173 older Icelandic adults [42% men; mean (standard deviation, SD) age of 80 (5) years] was performed to examine the distribution of estimated...
glomerular filtration rate (eGFR) from creatinine and cystatin C, the albumin-to-creatinine ratio (ACR), and CKD-related metabolic complications (hyperparathyroidism, anemia, hypoalbuminemia, increased anion gap, acidosis, hyperphosphatemia and hyperkalemia).

Results. There was substantial variability in eGFR [mean (SD) 64 (18) mL/min/1.73 m²] and ACR [median (interquartile range) 8 (5, 17) mg/g]. The prevalence (95% confidence interval) of reduced eGFR (<60 mL/min/1.73 m²), albuminuria (ACR >30 mg/g) and CKD (either reduced eGFR or albuminuria) was 40% (38–41), 14% (12–15) and 45% (43–47), respectively. The prevalence of complications was higher among those with versus without CKD: hyperparathyroidism (38 versus 15%), anemia (26 versus 14%), hypoalbuminemia (19 versus 13%), increased anion gap (9 versus 5%), acidosis (5 versus 1%); (P ≤ 0.02 for all), except hyperphosphatemia (1 versus 1%) and hyperkalemia (0% overall).

Conclusions. The burden of CKD and CKD-related complications is high among community-dwelling elderly Icelandic adults. The wide range of eGFR and ACR suggests heterogeneity in processes leading to CKD and that factors beyond aging contribute to the development of CKD in the elderly.

Keywords: albuminuria, chronic kidney disease, complications, elderly, prevalence

INTRODUCTION

Chronic kidney disease (CKD) is common in the elderly. In the USA, it is estimated that almost half of adults over the age of 70 years have CKD [1, 2]. CKD is a heterogeneous condition, characterized by a decrease in glomerular filtration rate (GFR) or markers of kidney damage, most commonly demonstrated by an increase in albuminuria [3, 4]. Both components of CKD—reduced GFR and albuminuria—are independently associated with major complications of CKD, including kidney failure, cardiovascular disease and all-cause mortality [5–8].

In addition to major events, CKD-related metabolic complications are common, including hyperparathyroidism, anemia, hypoalbuminemia, increased anion gap, acidosis, hyperphosphatemia and hyperkalemia. These complications are important in clinical care decisions, and new medications are available to treat some of them. The strong association of comorbid metabolic complications of CKD with lower estimated glomerular filtration rate (eGFR) has been established previously [9–16]. However, few studies evaluating associations with metabolic complications have focused on the elderly [10, 13, 14] or have incorporated both eGFR and albuminuria when defining CKD [9, 10, 15]. Prior studies were also limited by estimation of GFR only from serum creatinine [13, 14, 17–20], which may be biased by non-GFR determinants in the elderly.

The goal of the present analysis was a comprehensive description of the distribution of eGFR assessed from the combination of creatinine and cystatin C and the albumin-to-creatinine ratio (ACR) from spot urine samples, the prevalence of reduced eGFR, albuminuria and CKD, and associations with CKD-related metabolic complications in a large, representative Iceland cohort of elderly adults from the Age, Gene/Environment Susceptibility Reykjavik (AGES-Reykjavik) Study.

MATERIALS AND METHODS

Study participants

The AGES-Reykjavik Study is a community-based cohort study designed to prospectively examine the role of gene–environment interactions in the development of clinical and subclinical disorders in old age [21]. The first study visit in 2002–06 included 5764 participants recruited from a random sample of survivors of the Reykjavik Study, a prospective cohort study conducted between 1967 and 1996 in Iceland to study cardiovascular disease. In 2007–11, 3411 participants who attended the first study visit went to a second study visit, representing 71% of the survivors who attended the first visit [21, 22]. We selected measurements at Visit 2 for the present analysis because we measured cystatin C in all participants at Visit 2 (enabling more precise eGFR) and because measurements for CKD-related metabolic complications [serum intact parathyroid hormone (iPTH), bicarbonate, phosphate, chloride] were measured as part of an ancillary study to measure GFR in a subsample of Visit 2 participants in 2010–11 (AGES-Kidney). Of the 3411 participants who attended the second visit, the 3173 participants who had available serum and urinary assessments of kidney measures and serum measurements of hemoglobin and albumin were included in this analysis. Additional analyses related to hyperparathyroidism, increased anion gap, acidosis and hyperphosphatemia were performed in a subsample of this cohort in the AGES-Kidney ancillary study (n = 773). The study was approved by the Icelandic Bioethics Committee and institutional review boards at Tufts Medical Center and the National Institute on Aging. Written informed consent was obtained from all study participants.

Exposure assessment—kidney measures

Serum creatinine was assayed on a Roche Hitachi-P Module Automated Analyzer [Hoffman-La Roche, Ltd, Basel, Switzerland; coefficient of variation (CV) 2.5%]. Serum cystatin C was assayed on a Siemens ProSpec nephelometric analyzer (Siemens Healthcare Diagnostics, Deerfield, IL; CV of 4.0%) standardized to the International Federation for Clinical Chemists (IFCC) Working Group for the Standardization of Serum Cystatin C and the Institute for Reference Materials and Measurements (IRMM) certified reference materials [23–25]. Urinary albumin and creatinine were measured in a random spot urine sample and were assayed, respectively, on a ProSpec nephelometric analyzer (Dade Behring GMBH, Marburg, Germany; CV of 3.2%) and on a Roche Modular P Chemistry Analyzer (Roche Diagnostics, Indianapolis, IN; CV 4.3% at a concentration of 18.39 mg/dL and 1.5% at 96.57 mg/dL). Glomerular filtration rate was estimated (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2012 creatinine-cystatin C equation [26]. Urine albumin and creatinine was used to calculate urine ACR (mg/g). CKD was defined by eGFR <60 mL/min/1.73 m² or ACR >30 mg/g [27].
Outcome assessment—CKD-related complications

Serum sodium (CV 1.0%), potassium (CV 1.0%), chloride (CV 1.0%), bicarbonate (CV 5.0%), phosphorus (CV 2.2%) and albumin (CV 2.6% at a concentration of 3.14 g/dL and 2.5% at 4.01 g/dL) were assayed on a Roche Modular P Chemistry Analyzer (Roche Diagnostics, Indianapolis, IN). iPTH was measured in plasma on a Siemens Centaur chemiluminescent immunoassay (Siemens Healthcare Diagnostics, Deerfield, IL; CV of 20.8% in the 7–18 pg/mL range and 7.25% in the 118–158 pg/mL range). Hemoglobin was measured in whole blood on an automated cell counter, Coulter HmX AL Hematology Analyzer (Beckman Coulter, High Wycombe, UK; CV of 0.84%).

Hyperparathyroidism was defined as iPTH ≥70 pg/mL. Anemia was defined according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines as hemoglobin <12 g/dL in women and <13.5 g/dL in men [28]. Hypoalbuminemia was defined as serum albumin <3.5 g/dL. Anion gap was computed as the sum of serum chloride and bicarbonate subtracted from serum sodium and increased anion gap was defined as ≥14 mmol/L. Acidosis was defined as serum bicarbonate <21 mmol/L. Hyperphosphatemia was defined as serum phosphate ≥4.5 mg/dL. Hyperkalemia was defined as a serum potassium >5 mmol/L [9, 28, 29]. Hyperparathyroidism, anemia, hypoalbuminemia, acidosis and hyperphosphatemia were defined as in previous work in National Health and Nutrition Examination Survey (NHANES) [9].

Covariate assessment

Clinical and demographic covariates were assessed during the AGES-II-Reykjavik study visit. Body mass index (BMI, kg/m²) was calculated from weight and height measurements performed by trained clinic staff. Obesity was defined as a BMI ≥30 kg/m². Diabetes was defined as fasting glucose level ≥126 mg/dL or self-reported treatment by insulin, antidiabetic medication or with diet. Current smokers were defined as self-reported current use of cigarettes, pipes or cigars. Dyslipidemia was defined as triglycerides ≥150 mg/dL, low density lipoprotein (LDL)-cholesterol ≥130 mg/dL or high density lipoprotein (HDL)-cholesterol of <40 mg/dL (in men) or <50 mg/dL (in women).

Statistical analyses

Study sample characteristics were described overall and by eGFR and ACR category using the mean and standard deviation for normally distributed [median and interquartile range (IQR) for non-normally distributed] continuous variables and N (%) for categorical variables. The χ²-test (Fisher’s exact with small sample size) was used to test for differences among participants with CKD compared with those without. We estimated the prevalence of reduced eGFR, albuminuria and CKD, overall and in groups defined by age (<80, 80–84, ≥85 years), sex, diabetes status (yes, no), systolic blood pressure (<140, 140–159, ≥160 mmHg), BMI (<20, 20–24, 25–29, ≥30 kg/m²), dyslipidemia status (yes, no) and current smoking status (yes, no). We estimated the proportion of participants who fell within eGFR (≥90, 75–89, 60–74, 45–59, 30–44 and <30 mL/min/1.73 m²) and ACR categories (<10, 10–30 and >30 mg/g). We estimated the prevalence of CKD-related complications in the overall sample and across eGFR and ACR categories. We tested for trends in the prevalence of CKD-related complications across eGFR and ACR categories, except for complications with low numbers of events where tests of statistical trends could not be performed (acidosis, hyperphosphatemia and hyperkalemia). We estimated the prevalence [95% confidence interval (CI)] of hyperparathyroidism, anemia, hypoalbuminemia and increased anion gap as functions of continuous eGFR or ACR, respectively, modeled as restricted cubic splines (four knots) using logistic regression models. The restricted cubic splines were plotted between the 2.5 and 97.5 percentiles of the distribution of eGFR and ACR. Models were (i) unadjusted, and (ii) adjusted for age, sex, diabetes, current smoking, BMI, systolic blood pressure and LDL-cholesterol. Prevalence estimates with continuous eGFR or ACR were not determined for acidosis and hyperphosphatemia due to the small number of events leading to unstable estimates. We calculated the population attributable risk as the difference in the prevalence of complications in the overall population and the prevalence of complications in those without CKD. Using quantile regression, we graphically evaluated the distribution (median, 5th, 95th percentiles) of serum iPTH, hemoglobin, albumin, anion gap, bicarbonate, phosphate and potassium measurements across the range of eGFR and ACR values. Analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC, www.sas.com) and R (version 3.1.0; Free Software Foundation Inc., www.r-project.org) using the RMS package [30].

RESULTS

Study sample characteristics

The clinical characteristics of study participants are summarized in Table 1. Participants were on average 80.1 years old, 42% were male and 12% had diabetes. The mean ± SD for eGFR was 63.9 ± 17.5 mL/min/1.73 m². The median (IQR) for ACR was 8.2 (5.2–17.5) mg/g.

Prevalence of CKD, reduced eGFR and albuminuria

There is a wide distribution of participants across eGFR and ACR categories (Table 2). The prevalence (95% CI) of reduced eGFR, albuminuria and CKD (either reduced eGFR or albuminuria) was 40% (38–41), 14% (12–15) and 45% (43–47), respectively. The prevalence of reduced eGFR was associated with older age, female sex, diabetes, low LDL-cholesterol, low HDL-cholesterol, high triglycerides and higher BMI (Supplementary data, Figure S1). The prevalence of albuminuria was associated with older age, male sex, diabetes, higher systolic blood pressure, current smoking, low LDL-cholesterol, low HDL-cholesterol and low BMI (Supplementary data, Figure S1).

Prevalence of CKD-related complications

Hyperparathyroidism, anemia and hypoalbuminemia were common (24.1, 19.3 and 15.3%, respectively), whereas increased anion gap, acidosis and hyperphosphatemia were uncommon (6.2, 2.2 and 1.0%, respectively) and no participants had hyperkalemia (Table 3). All complications, with the exception of hyperphosphatemia and hyperkalemia, were...
### Table 1. Population characteristics, overall and stratified by eGFR values and ACR categories

<table>
<thead>
<tr>
<th>Overall</th>
<th>eGFR categories (mL/min/1.73 m²)</th>
<th>ACR categories (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥90</td>
<td>75–89</td>
</tr>
<tr>
<td>N (%)</td>
<td>3173</td>
<td>191 (6)</td>
</tr>
<tr>
<td>Age, years</td>
<td>80.1 ± 4.8</td>
<td>77.5 ± 3.6</td>
</tr>
<tr>
<td>Male, N (%)</td>
<td>1347 (42)</td>
<td>94 (49)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.0 ± 4.4</td>
<td>26.0 ± 4.2</td>
</tr>
<tr>
<td>Diabetes, N (%)</td>
<td>380 (12)</td>
<td>27 (14)</td>
</tr>
<tr>
<td>Current smoker, N (%)</td>
<td>264 (8)</td>
<td>25 (13)</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>144 ± 21</td>
<td>147 ± 19</td>
</tr>
<tr>
<td>LDL, mg/dL</td>
<td>120 ± 40</td>
<td>119 ± 37</td>
</tr>
<tr>
<td>HDL, mg/dL</td>
<td>62 ± 17</td>
<td>67 ± 19</td>
</tr>
<tr>
<td>Triglycerides, median (IQR), mg/dL</td>
<td>95 (74, 122)</td>
<td>76 (60, 100)</td>
</tr>
</tbody>
</table>

**Kidney measures**

| Serum creatinine, mg/dL | 1.2 ± 0.4 | 0.8 ± 0.1 | 0.9 ± 0.1 | 1.1 ± 0.2 | 1.3 ± 0.2 | 1.6 ± 0.3 | 2.3 ± 0.7 | 1.1 ± 0.3 | 1.2 ± 0.4 | 1.4 ± 0.6 |
| Serum cystatin C, mg/L | 1.1 ± 0.3 | 0.7 ± 0.1 | 0.8 ± 0.1 | 0.9 ± 0.1 | 1.1 ± 0.1 | 1.5 ± 0.2 | 2.1 ± 0.5 | 1.0 ± 0.3 | 1.1 ± 0.3 | 1.3 ± 0.5 |
| eGFR, mL/min/1.73 m² | 63.9 ± 17.5 | 95.5 ± 4.6 | 81.4 ± 4.3 | 67.5 ± 4.3 | 53.2 ± 4.4 | 38.8 ± 4.4 | 24.4 ± 4.9 | 66.0 ± 16.3 | 63.7 ± 17.7 | 55.0 ± 19.1 |
| ACR, median (IQR), mg/g | 8.2 (5.2, 16.7) | 7.4 (5.2, 14.0) | 7.6 (5.1, 12.7) | 7.5 (5.1, 14.0) | 8.7 (5.3, 18.4) | 11.3 (5.8, 29.8) | 21.6 (8.3, 101.7) | 5.7 (4.4, 7.3) | 15.4 (12.0, 20.3) | 63.9 (40.0, 131.4) |

**Continuous data are presented as mean ± standard deviation, unless otherwise indicated. ACR, urine albumin-to-creatinine ratio; BMI, body mass index; SBP, systolic blood pressure; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol; eGFR, glomerular filtration rate estimated using the CKD-EPI 2012 creatinine-cystatin C equation; IQR, interquartile range.**

*N = 773.*
significantly more common among participants with than in those without CKD (Table 3, P ≤ 0.02). Excess risk for hyperparathyroidism, anemia, hypoalbuminemia, increased anion gap and acidosis associated with CKD in the overall population was 8.9, 5.4, 2.7, 1.7 and 1.6%, respectively.

The prevalence of hyperparathyroidism, anemia, hypoalbuminemia and increased anion gap was significantly higher in lower eGFR categories (all P-trend < 0.0001). For associations with continuous eGFR (Figure 1), there is an apparent threshold of 70 mL/min/1.73 m² for hypoalbuminemia and hyperparathyroidism and 60 mL/min/1.73 m² for anemia and increased anion gap, below which prevalence rises linearly (Figure 1); results were similar when unadjusted and adjusted for age, sex, diabetes, current smoking, BMI, systolic blood pressure and LDL-cholesterol. In sensitivity analyses using creatinine-only based eGFR (eGFRcr), the dose-response curves with continuous eGFRcr were similar although more suggestive of a J-shaped association (Supplementary data, Figure S2). The median, 5th and 95th percentile for serum levels of each complication marker across the range of continuous eGFR values are presented in Supplementary data, Figure S3.

The prevalence of hyperparathyroidism (P-trend = 0.009), anemia (P-trend < 0.0001) and hypoalbuminemia (P-trend = 0.02), but not increased anion gap (P-trend = 0.22), was significantly higher with higher ACR category. The prevalence of acidosis and hyperphosphatemia was also higher in those in higher ACR categories, but tests of statistical trend could not be performed due to small event counts. For continuous ACR (Figure 2), the prevalence of hyperparathyroidism rose gradually with higher ACR values. The prevalence of anemia is slightly higher between ACR values of 5 and 30 mg/g and remained stable at higher ACR levels. The prevalence of hypoalbuminemia and increased anion gap were stable at lower ACR values and higher at ACR values higher than ~30 mg/g. The median, 5th and 95th

Table 2. Prevalence of ACR and eGFR categories, N (%)

<table>
<thead>
<tr>
<th>eGFR categories (mL/min/1.73 m²)</th>
<th>ACR categories (mg/g)*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥90</td>
<td>&lt;10</td>
<td>118 (3.7)</td>
</tr>
<tr>
<td>75–89</td>
<td>30–30</td>
<td>159 (1.9)</td>
</tr>
<tr>
<td>60–74</td>
<td>&gt;30</td>
<td>14 (0.4)</td>
</tr>
<tr>
<td>45–59</td>
<td>&lt;10</td>
<td>191 (6.0)</td>
</tr>
<tr>
<td>30–44</td>
<td>30–30</td>
<td>690 (21.7)</td>
</tr>
<tr>
<td>&lt;30</td>
<td>&gt;30</td>
<td>1035 (32.6)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>3173 (100)</td>
</tr>
</tbody>
</table>

Note: Shaded box represents participants with CKD [45.2%, 95% CI (43.4%–46.9%)].

ACR, urine albumin-to-creatinine ratio; eGFR, glomerular filtration rate in mL/min/1.73 m² estimated using the CKD-EPI 2012 creatinine-cystatin C equation. SI conversion factors: to convert ACR from mg/g to mg/mmol, multiply by 0.113.

ACR values higher than 30 mg/g. The median, 5th and 95th percentile for serum levels of each complication marker across the range of continuous eGFR values are presented in Supplementary data, Figure S3.

The prevalence of hyperparathyroidism (P-trend = 0.009), anemia (P-trend < 0.0001) and hypoalbuminemia (P-trend = 0.02), but not increased anion gap (P-trend = 0.22), was significantly higher with higher ACR category. The prevalence of acidosis and hyperphosphatemia was also higher in those in higher ACR categories, but tests of statistical trend could not be performed due to small event counts. For continuous ACR (Figure 2), the prevalence of hyperparathyroidism rose gradually with higher ACR values. The prevalence of anemia is slightly higher between ACR values of 5 and 30 mg/g and remained stable at higher ACR levels. The prevalence of hypoalbuminemia and increased anion gap were stable at lower ACR values and higher at ACR values higher than ~30 mg/g. The median, 5th and 95th
percentile for serum levels of each complication marker across the range of continuous ACR values are presented in Supplementary data, Figure S4.

DISCUSSION

It is well known that CKD is common in the elderly, but the distribution and prevalence of reduced eGFR, albuminuria and CKD-related metabolic complications in this population have not been well characterized. In our sample of community dwelling elderly Icelandic adults from the AGES-Reykjavik Study, the prevalence of overall CKD was high with reduced eGFR more common than albuminuria, but there was substantial variation in both eGFR and ACR. The prevalence of seven CKD-related metabolic complications varied across this population, with higher prevalence estimates for hyperparathyroidism, anemia and hypoalbuminemia than for increased anion gap, acidosis and hyperphosphatemia. The prevalence of these complications tended to be higher with lower eGFR and higher ACR. In contrast to other metabolic complications, hypokalemia was not present in this cohort.

Our findings in elderly Icelandic adults showed similar trends with increasing prevalence of metabolic complications at lower eGFR levels [9, 10, 13]. In contrast, studies in the general US adult population from the NHANES had shown J-shaped associations of metabolic complications with creatinine-based eGFR, with higher prevalence ratios of hyperparathyroidism, anemia, hypoalbuminemia, acidosis and hyperphosphatemia observed for both low and high eGFR values [9]. This J-shaped association with increased prevalence at high eGFR values is thought to reflect low creatinine generation in persons with muscle wasting and therefore overestimation of GFR in this subset of the population. Given that muscle wasting occurs with aging, one might expect that these J-shaped associations would be more pronounced in the elderly. However, we did not find evidence of J-shaped associations of metabolic complications with eGFR in this elderly Icelandic cohort, with prevalence estimates remaining stable until eGFR values fell below ∼60–70 mL/min/1.73 m². Similarly, separate analyses restricted to elderly NHANES participants also did not show J-shaped associations for these complications [13]. This may reflect a survivor bias, as our study sample for eGFR and ACR that do not meet the criteria for CKD, despite their advanced age, suggesting that factors other than age are associated with lower eGFR and higher ACR. In addition, lower eGFR and higher ACR also remain associated with increased prevalence of several metabolic complications even with adjustment for age, indicating that abnormalities in kidney measures observed in the elderly are markers of important clinical complications beyond the effect of normal aging.

FIGURE 1. Prevalence estimates of hyperparathyroidism, anemia, hypoalbuminemia and increased anion gap across continuous eGFR values.
included elderly individuals who were healthy enough to attend the AGES examination visit and are likely healthier than the overall elderly population in Iceland, although NHANES is also selected to be representative of the civilian, non-institutionalized US population and does not capture elderly US adults who live in nursing homes or other facilities. An alternative explanation is that we did not observe a J-shaped association with eGFR because we used both creatinine and cystatin C to calculate eGFR, minimizing the overestimation that occurs in persons with muscle wasting when using estimation equations that are only based on creatinine. Models did suggest a more J-shaped association in sensitivity analyses with eGFR estimated from creatinine alone, but CIs for prevalence estimates showed wide overlap with our primary analyses. It is possible that a more pronounced J-shaped association would be observed with a higher number of participants with high eGFR.

For albuminuria, we also observed similar trends for metabolic complications when compared with the general US adult population from NHANES [9], with higher prevalence estimates of hyperparathyroidism, anemia and hypoalbuminemia and relatively stable prevalence estimates for hyperphosphatemia with higher ACR. Overall associations of metabolic complications with higher ACR were also more modest than observed with lower eGFR. Unlike in NHANES the prevalence of acidosis was low in our cohort and did not appear to change substantially with higher ACR.

Strengths of our study include that this is a well-characterized sample of the elderly population from Iceland and that both creatinine and cystatin C were measured in this cohort, allowing us to estimate GFR using the most accurate currently available estimation equation for eGFR [26]. Limitations include that prevalence estimates are based on single assessments of kidney measures and markers of metabolic complications, which could lead to over estimates, in particular for albuminuria. Bicarbonate, iPTH, phosphate and chloride were measured in a subsample of participants (n = 773), which limited some statistical analyses due to low event rates. With the cross-sectional design, we are unable to evaluate whether observed associations of kidney measures and metabolic complications are causal or reflect shared upstream biological factors. Our study sample included participants who were healthy enough to attend the second AGES visit, which may impact generalizability to the overall elderly population in Iceland. However, this suggests that our observed associations reflect conservative estimates that underestimate the overall prevalence of CKD and CKD complications in elderly Icelandic adults. Finally, as our study population consists of elderly Caucasian adults from Iceland it may not generalize to populations with different racial/ethnic backgrounds.

In summary, the burden of CKD and CKD-related complications is high among community dwelling elderly Icelandic adults. Our findings have the potential to inform clinical care and treatment decisions related to kidney function in aging populations. The substantial variability in kidney measures across eGFR and ACR categories suggests that factors beyond aging influence kidney function. Future studies are needed to identify the additional factors that lead to heterogeneity in processes that contribute to the development of CKD in the elderly.

FIGURE 2. Prevalence estimates of hyperparathyroidism, anemia, hypoalbuminemia and increased anion gap across continuous ACR values.
SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

ACKNOWLEDGEMENTS

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CONFLICTS OF INTEREST STATEMENT

Preliminary results of this research were presented in abstract form at the Annual Meeting of the American Society of Nephrology, November 11–16, 2014, Philadelphia, PA and the American Heart Association Epilepsy Lifestyle 2015 Scientific Sessions, March 3–6, 2015, Baltimore, MD. L.A.I. reports funding to Tufts Medical Center for research and contracts with the National Institutes of Health, National Kidney Foundation, Pharmalink AB and Gilead Sciences, a consulting agreement with Otsuka, and has a provisional patent (Coresh, Inker and Levey) filed 8/15/2014—precise estimation of GFR from multiple biomarkers (licensing under negotiations). A.S.I. reports funding to Tufts Medical Center for research and contracts with the National Institutes of Health, National Kidney Foundation, Amgen, Pharmalink AB, Gilead Sciences, and has a provisional patent (Coresh, Inker and Levey) filed 8/15/2014—precise estimation of GFR from multiple biomarkers (licensing under negotiations). A.O., M.C.F., H.T., V.G., O.I., H.G., E.F.G. and G.E. declare that they have no conflicts of interest.


REFERENCES

Effects of blood pressure on renal and cardiovascular outcomes in Asian patients with type 2 diabetes and overt nephropathy: a post hoc analysis (ORIENT-blood pressure)

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ABSTRACT

Background. Blood pressure (BP) control may have different effects on cardiovascular (CV) and renal outcomes in diabetes. We examined the impact of systolic BP (SBP) on renal and CV outcomes in a post hoc analysis in the Olmesartan Reducing Incidence of Endstage Renal Disease in Diabetic Nephropathy Trial.

Methods. We stratified mean follow-up SBP into three categories (≤130, 131–140 and >140 mmHg) and used a Cox regression model to estimate the hazard ratio (HR, 95% confidence interval) for the outcomes. The composite renal outcome was doubling of serum creatinine, end-stage renal disease and all-cause death. The composite CV outcome included CV death, nonfatal stroke, nonfatal myocardial infarction, hospitalization for unstable angina or heart failure, revascularization and lower extremity amputation. We also compared the slope of estimated glomerular filtration rate (eGFR) in all three groups.

Results. After a mean follow-up period of 3.2 years, the follow-up SBP was linearly associated with risk of renal outcomes in all 566 patients. In patients with heavy proteinuria (≥1 g/gCr), a follow-up SBP > 130 mmHg was associated with an HR of 2.33 (1.62–3.36) for renal outcomes with referent to SBP ≤ 130 mmHg. In patients without history of CV disease, a follow-up SBP > 140 mmHg was associated with an HR of 2.04 (1.23–3.40) for CV outcomes with referent to SBP < 140 mmHg. The median (interquartile range) slopes of eGFR were −3.27 (−6.90, −1.63), −4.53 (−8.08, −2.29) and −7.13 (−10.90, −3.99) mL/mg/year in patients with SBP ≤ 130, 131–140 and > 140 mmHg, respectively (P = 0.008 between ≤130 and 131–140, P < 0.001 between ≤130 and > 140 mmHg).

Conclusion. In Asian type 2 diabetic patients with chronic kidney disease and heavy proteinuria, reduction of SBP ≤ 130 mmHg was associated with greater renoprotection than cardioprotection. However, our results emphasize the need to individualize BP targets in type 2 diabetes.

Keywords: cardiovascular outcome, diabetic nephropathy, proteinuria, renal outcome, systolic blood pressure