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Agreement between Chronic Kidney Disease Epidemiological Collaboration and Berlin Initiative Study equations for estimating glomerular filtration rate in older people: The Invecchiare in Chianti (Aging in Chianti Region) study

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Abstract

Aim—The aim was to investigate to what extent chronic kidney disease (CKD) can be staged interchangeably by Chronic Kidney Disease Epidemiological Collaboration (CKD-EPI) and by Berlin Initiative Study (BIS) equations, and to verify whether cystatin C can improve concordance between formulas.

Methods—Our series consisted of 828 community-dwelling individuals aged 65 years or older enrolled in the Invecchiare in Chianti Study (“Aging in the Chianti Region”). Estimated glomerular filtration rate was calculated using the creatinine-based CKD-EPI, creatinine/cystatin C-based CKD-EPI, creatinine-based BIS and creatinine/cystatin C-based BIS equations. Agreement and sources of discrepancy between equations in identifying people with different degrees of kidney dysfunction was investigated by κ statistic and Bland–Altman plots.

Results—Overall, CKD-EPI values were higher than that obtained with BIS equations, especially for $eGFR = 30–60$ mL/min/1.73 m². A total of 191 out of 828 participants were classified in stage 2 by the creatinine-based CKD-EPI and in stage 3a by the creatinine-based BIS equation, whereas 123 participants were classified in stage 2 by creatinine/cystatin C-based CKD-EPI and in stage 3a by the creatinine/cystatin C-based BIS equation. A total of 27 participants were classified in stage 3a by creatinine-based CKD-EPI and in stage 3b by creatinine-based BIS

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Disclosure

The authors declare no conflict of interest.

Supporting Information

Additional supporting information may be found in the online version of this article at the publisher’s web site.

equation, whereas 18 were classified as stage 3a by creatinine/cystatin C-based CKD-EPI and stage 3b by the creatinine/cystatin C-based BIS equation.

Conclusions—Despite a fair overall concordance, the CKD-EPI and BIS equations cannot be considered interchangeable to assess estimated glomerular filtration rate in older people, and using creatinine/cystatin C-based rather than creatinine-based equations only marginally improves the concordance between CKD-EPI and BIS. Disagreement between equations might significantly impact the applications of stage-specific measures for managing CKD among older people.

Keywords

Berlin Initiative Study; chronic kidney disease; Chronic Kidney Disease Epidemiological Collaboration; estimated glomerular filtration rate; misclassification

Introduction

Chronic kidney disease (CKD) increases in prevalence with age and is associated, with important cardiovascular and metabolic chronic conditions, among others. It dramatically impacts health status and survival in the general population, as well as in selected populations.^{1,2} Timely detection of CKD allows for the contrast of some pathogenetic mechanisms, such as uncontrolled hypertension or, in diabetic kidney, glomerular overflow, which slows the progression of kidney damage.³ Importantly, it also allows for the dosage of several drugs to be tailored to kidney function, and CKD staging is the basis for stage-specific non-pharmacological and pharmacological measures.⁴ Unfortunately, the diagnosis of CKD is frequently missed. Indeed, a retrospective analysis of 9307 diabetic patients showed that 54.1% had stage 1–5 CKD based on estimated glomerular filtration rate (eGFR) and albuminuria, but just 12.1% were identified as having CKD by their primary care physicians.⁵ This likely reflects a lack of awareness of CKD, especially of its earlier stages, as a major health problem. Furthermore, sarcopenia, which is common in frail older adults, could account for decreased production of creatine and the ensuing low levels of serum creatinine, even despite depressed GFR.⁶ Accordingly, efforts have been prompted to identify depressed GFR, mainly in older and frail people. To this aim, several equations to calculate eGFR have been developed and tested.^{7–9}

Serum creatinine has a variable weight in these equations, but serum cystatin C (CysC) has been added to creatinine or substituted for it in recently developed equations.^{9,10} CysC is considered a reliable index of metabolically active cells, and is almost completely independent from tubular secretory and absorptive mechanisms.¹¹ However, CysC has not become widely used in clinical practice because of its cost and, thus, limited availability.

Equations estimating eGFR have been progressively refined, and the Chronic Kidney Disease Epidemiological Collaboration (CKD-EPI) is currently recommended,¹² but very recently the Berlin Initiative Study (BIS) equation has been developed to be used in older people,⁹ and it has been validated.¹³ This equation has been recommended for estimating eGFR in older patients with mild to moderate CKD. However, subsequent studies have cast doubt on this conclusion. Indeed, Fan *et al.* showed that BIS does not outperform CKD-EPI in predicting GFR measured by iothexol clearance as the reference standard in older people,

¹⁴ and similar findings were obtained in community-dwelling individuals aged 80 years or older.¹⁵ Additionally, Koppe *et al.* showed that creatinine-based CKD-EPI had a lower bias in predicting inulin clearance compared with the creatinine-based BIS equation (BIS_{cre}) in older patients with severe CKD.¹⁶ Thus, the current evidence suggests that CKD-EPI may be useful in older people even if not specifically developed in an older population.

Based on these findings, we reasoned that further useful information can be gained by comparing the respective classificatory properties of these equations with regard to CKD staging. Indeed, classifying a given patient into different CKD stages would imply different measures to treat CKD. Thus, a poor concordance between equations, whichever is their respective accuracy in predicting measured GFR, would have practical clinical implications.

Therefore, we evaluated to what extent CKD can be staged interchangeably by CKD-EPI and by BIS equations in people aged 65 years or older. We also aimed to assess the source and the clinical implication of discrepancy, if any. Finally, based on the alleged lesser classificatory added value of CysC in older adults, we aimed to verify to what extent CysC can improve concordance between formulas.¹⁷

Methods

Data source

We used data from the Invecchiare in Chianti (Aging in Chianti Region; InCHIANTI) study, which was designed to investigate the factors contributing to the decline of mobility in older persons.¹⁸ The participants in the study were randomly selected from the populations of two town areas in the Chianti region: Greve in Chianti and Bagno a Ripoli. The Italian National Institute of Research and Care on Aging ethical committee ratified the study protocol. Participants received an extensive description of the study, and signed an informed participation consent that included permission to carry out analysis on the biological specimens collected and stored. For those unable to fully consent because of cognitive or physical problems, surrogate consent was obtained from a close relative. The eligible participants were interviewed at their homes by trained study researchers using a structured questionnaire aimed at carrying out a comprehensive geriatric assessment. The interview was followed by a physical examination at the study clinic. Participants were followed up with evaluations at 3, 6 and 9 years. Only data collected during the enrollment interview were used for the present study.

Among 1453 participants enrolled in the InChianti database, 939 were aged 65 years or older. Of them, 828 had both serum creatinine and CysC measured at the baseline, and were included in the study.

Laboratory assays

Blood samples obtained after the patient had fasted for 12 h and rested for at least 15 min were centrifuged and stored at –80 until analyzed. Serum creatinine was measured by the modified Jaffé method standardized against gas chromatography (isotope dilution IDMS) mass spectrometry (Roche Diagnostics, GmbH, Mannheim, Germany). Serum CysC was measured using a particle-enhanced immunonephelometric assay (N Latex Cystatin C kit;

Dade Behring, Marburg, Germany). The eGFR was calculated using the following equations:

$$\begin{aligned}
 &\text{CKD- EPI}_{\text{cre}}^8: \\
 &\text{Female } (\text{Scr} \leq 0.7) \text{ eGFR} = 144 \times (\text{Scr}/0.7)^{-0.329} \times (0.993)^{\text{Age}} \\
 &\quad (\text{Scr} > 0.7) \text{ eGFR} = 144 \times (\text{Scr}/0.7)^{-1.209} \times (0.993)^{\text{Age}} \\
 &\text{Male } (\text{Scr} \leq 0.9) \text{ eGFR} = 141 \times (\text{Scr}/0.9)^{-0.411} \times (0.993)^{\text{Age}} \\
 &\quad (\text{Scr} > 0.9) \text{ eGFR} = 141 \times (\text{Scr}/0.9)^{-1.209} \times (0.993)^{\text{Age}} \\
 &\text{CKD- EPI}_{\text{cre-cys}}^{10}: \\
 &\text{Female } (\text{Scr} \leq 0.7) (\text{Scys} \leq 0.8) \text{ eGFR} = 130 \times (\text{Scr}/0.7)^{-0.248} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}] \\
 &\quad (\text{Scr} \leq 0.7) (\text{Scys} > 0.8) \text{ eGFR} = 130 \times (\text{Scr}/0.7)^{-0.248} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}] \\
 &\text{Female } (\text{Scr} > 0.7) (\text{Scys} \leq 0.8) \text{ eGFR} = 130 \times (\text{Scr}/0.7)^{-0.601} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}] \\
 &\quad (\text{Scr} > 0.7) (\text{Scys} > 0.8) \text{ eGFR} = 130 \times (\text{Scr}/0.7)^{-0.601} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}] \\
 &\text{Male } (\text{Scr} \leq 0.9) (\text{Scys} \leq 0.8) \text{ eGFR} = 135 \times (\text{Scr}/0.9)^{-0.207} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}] \\
 &\quad (\text{Scr} \leq 0.9) (\text{Scys} > 0.8) \text{ eGFR} = 135 \times (\text{Scr}/0.9)^{-0.207} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}] \\
 &\text{Male } (\text{Scr} > 0.9) (\text{Scys} \leq 0.8) \text{ eGFR} = 135 \times (\text{Scr}/0.9)^{-0.601} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}] \\
 &\quad (\text{Scr} > 0.9) (\text{Scys} > 0.8) \text{ eGFR} = 135 \times (\text{Scr}/0.9)^{-0.601} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}] \\
 &\text{BIS}_{\text{cre}}^9: 3736 \times \text{creatinine}^{-0.87} \times \text{age}^{-0.95} \times 0.82 (\text{if female}) \\
 &\text{BIS}_{\text{cre-cys}}^9: 767 \times \text{cystatin C}^{-0.61} \times \text{creatinine}^{-0.40} \times \text{age}^{-0.57} \times 0.87 (\text{if female})
 \end{aligned}$$

Study variables

Age, sex, and variables potentially affecting kidney function estimates and agreement between equations were considered in the analysis. As bodyweight might represent a potential source of disagreement between equations,¹⁹ actual bodyweight (i.e. the weight measured at the time of enrollment) and ideal bodyweight (as calculated by the Devine equation),²⁰ as well as body mass index were considered in the analysis. Smoking habits and selected diagnoses, including hypertension, heart failure, stroke, transient ischemic attack, peripheral arterial disease, chronic liver disease, chronic obstructive pulmonary disease, cancer, dementia, Parkinson's disease, hip fracture, metabolic syndrome, diabetes and dysthyroidism were also included in the analysis. Finally, given that reduced muscle mass can significantly affect serum creatinine, muscle density and muscle cross-sectional area measured at 66% of tibial length were also considered a potential source of disagreement between equations.²¹

Depressive symptoms were assessed using the Center for Epidemiological Studies-Depression scale.²² Cognitive status was assessed using the age- and education-adjusted Mini-Mental State Examination score.²³ Self-reported degree of disability was rated using the number of lost basic activities of daily living.²⁴

Analytic approach

First, we analyzed the demographic and clinical characteristics of participants, and calculated the prevalence of the selected disease.

Bland-Altman plots were generated to plot the difference between CKD-EPI- and BIS-based eGFR against the mean of the two estimates. To investigate the impact of equation variables (i.e. age, serum creatinine and CysC), bodyweight, muscle area, and density on

difference between CKD-EPI and BIS estimates, we used a graphic approach plotting the difference of the values obtained by the two equations on the value of the variable of interest and using local regression techniques to fit a non-parametric curve smoothing the relationship between the two variables.

Therefore, the prevalence of CKD stages obtained with different equations was investigated. The κ statistic was used to quantify the agreement between equations in identifying people with different degrees of kidney dysfunction (eGFR >90, stage 1; 89.9–60, stage 2; 59.9–45, stage 3a; 44.9–30, stage 3b; and <30 mL/min/1.73 m², stage 4–5).⁴ Analysis was stratified by age, sex, smoking habits, diabetes, cognitive impairment and dependency in at least one BADL.

All analyses were carried out separately for creatinine-based and creatinine/cystatin-based equations.

Statistical analysis was carried out using SPSS Statistical Software Package for Windows version 18.0 (SPSS, Chicago, IL, USA).

Results

Demographic and clinical features of participants included in the analysis are reported in Table 1. Overall, the general health status of the studied population was good, as it can be derived from cognitive, affective and functional status. Hypertension was the most frequent diagnosis, followed by metabolic syndrome and diabetes, whereas the prevalence of highly disabling conditions (e.g. stroke, heart failure, chronic obstructive pulmonary disease, cancer) was low. CKD-EPI equations provided higher eGFR values compared with BIS equations.

Compared with the 828 participants included in the analysis, the 111 individuals excluded because of missing serum creatinine and/or CysC were of similar age (73.8 ± 6.2 , $P=0.345$), were more frequently male (57.7%, $P=0.003$), had higher actual bodyweight (71.3 ± 14.0 , $P=0.037$) and ideal bodyweight (55.6 ± 10.4 , $P=0.003$), and lower Center for Epidemiological Studies-Depression scale score (9.9 ± 7.3 , $P=0.001$).

Both CKD-EPI equations provided higher eGFR values compared with BIS equations, and this was particularly evident in the range of CKD stages 3a and 3b, and with creatinine-based CKD-EPI (CKD-EPI_{cre}; Fig. 1). With regard to creatinine/CysC-based equations, the difference was almost constant across age, but the greatest difference was observed for creatinine values <1.0 mg/dL and for CysC values <1.5 mg/L. The difference between CKD-EPI_{cre} and creatinine-based BIS (BIS_{cre}) was higher than that observed with creatinine/CysC-based equations, and rose with increasing age. Even in this case, the greatest difference was observed for creatinine values <1.0 mg/dL and for CysC values <1.5 mg/L (see Fig. S1).

The difference between creatinine/CysC-based CKD-EPI (CKD-EPI_{cre-cys}) and BIS (BIS_{cre-cys}) according to body mass index, actual bodyweight/ideal bodyweight ratio, muscle

area, and muscle density (see Fig. S2) was lower than that observed between CKD-EPI_{cre} and BIS_{cre} (see Fig. S3).

Stages 3a and 3b were much more prevalent when using BIS equations compared with CKD-EPI equations. For instance, the prevalence of stage 2 was 72.6% according to CKD-EPI_{cre} and 55.7% according to BIS_{cre}; the corresponding values for stage 3a were 17.1% and 37.0%, and for stage 3b were 1.3% and 4.6%, respectively.

Overall, κ values were 0.39 for CKD-EPI_{cre} versus BIS_{cre}, and 0.48 for CKD-EPI_{cre-cys} versus BIS_{cre-cys}, respectively. Overall, 191 out of 828 participants were classified in stage 2 by the CKD-EPI_{cre} equation and in stage 3a by the BIS_{cre} equation. Disagreement between CKD-EPI_{cre-cys} and BIS_{cre-cys} was slightly less frequent. In-deed, 123 out of 828 participants were classified in stage 2 by the CKD-EPI_{cre-cys} equation and in stage a by the BIS_{cre-cys} equation. Relative misclassification in CKD stages 3b and 3a was less frequent. A total of 27 participants were classified in stage 3a by CKD-EPI_{cre} and in stage 3b by BIS_{cre}, whereas 18 out of 828 patients were classified as stage 3a by the CKD-EPI_{cre-cys} equation and in stage 3b by the BIS_{cre-cys} equation (Table S1).

The observed percentage of relative misclassification in CKD stages 3b, 3a and 2 was higher among older participants (Table 2), women (Table 3) and participants with dependency in at least one BADL (Table 4). Diabetes (Table S2), smoking habits (Table S3) and cognitive impairment (Table S4) had less impact on the percentage of disagreement.

Discussion

The present findings show that the agreement between CKD-EPI and BIS formulas, with or without CysC, is fair in the upper and lower range of eGFR, whereas it worsens in the middle range. Thus, it is evident that selecting older adults for diagnostic and therapeutic interventions related to CKD stage changes depending on whether the BIS or the CKD-EPI formula is used, and this difference increases if creatinine-based and not creatinine/cystatin C-based formulas are used to estimate eGFR.

Disagreement between eGFR equations has been previously reported. In the general population, CKD-EPI_{cre} and Modification of Diet in Renal Disease equations showed an only fair agreement ($\kappa = 0.50$), similar to that obtained comparing CKD-EPI_{cre} and CKD-EPI_{cre-cys} ($\kappa = 0.53$).²⁵ Prevalence estimates of eGFR <60 in people aged 85 years or more participating in the Health and Anemia Study were 84.4% with BIS_{cre} and 53.6 % with CKD-EPI_{cre}, but a formal analysis of agreement between equations was not carried out in that study.²⁶ Finally, age, sex, weight and study setting were previously reported to represent important sources of discrepancy between equations.¹⁹ However, the present study differs from previous studies, as it aimed to estimate the agreement between equations only in terms of CKD staging; that is, in the perspective of the practicing clinician. Thus, its final aim was to assess the impact of the discrepancy on clinical practice given that well-defined therapeutic measures are recommended starting from CKD stage 3.⁴

In the present study, the discrepancy was greater in the very old and in people with dependency in at least one BADL; that is, in patients commonly plagued with frailty,

sarcopenia and multimorbidity. Relative misclassification is also more common in women, which might partly reflect the older age of women and partly the accelerated age-related loss of muscle mass in women. However, the latter factor might have a lesser explanatory role given that the concordance between formulas including CysC only to some extent was better than that between creatinine-based formulas in women. This suggests that body composition does not play a primary role in conditioning the concordance between creatinine-based and creatinine/CysC-based formulas, or that CysC has major limits in such a population. Indeed, being released by all nucleated cells, CysC is considered a proxy of the metabolically active population of cells.¹¹ However, CysC levels are variously affected by dysthyroidisms, corticosteroid therapy and selected cancers.²⁷ Interestingly, both hypothyroidism and hyperthyroidism are more common in women, and their prevalence increases with age.²⁸ Indeed, in our population, dysthyroidism was more prevalent in women (5.3%) than in men (0.8%, $P < 0.001$). Furthermore, immunological diseases requiring corticosteroid therapy are more prevalent in women.²⁸ This might contribute to explaining why the rate of concordance between creatinine/CysC- and creatinine-based equations was greater in women than in men; that is, CysC had a lesser impact on the concordance between formulas in the population more exposed to factors limiting its classificatory impact.

Whatever the mechanisms underlying misclassification are, they have important clinical implications in terms of potentially defective identification, staging and management of CKD, especially in stage 3 CKD. Given the high prevalence of stage 3 CKD, and the highly variable risk of mortality and other negative outcomes in this group, current guidelines include a distinction between CKD stage 3a and 3b.⁴ The risk associated with stage 3a CKD in older patients is still debated,²⁹ and the GFR threshold at which the risk of mortality increases might be lower among older patients compared with younger patients.³⁰ Additionally, older people with eGFR < 60 mL/min/1.73 m² show a slow progression of CKD.³¹ However, current guidelines do not calibrate the definition of CKD for age, and suggest many stage-specific therapeutic measures.⁴

Misclassification also poses important issues in the management of medications cleared by the kidneys, especially among older patients with multiple chronic diseases treated with polypharmacy regimens. As an example, the vast majority of hypoglycemic medications (including insulin) are cleared by the kidneys, and guideline recommendations suggest careful dosing of metformin, sulphonylureas, glucagon-like peptide-1 receptor agonists, dipeptidyl peptidase-4 inhibitors (excluding linagliptin) and sodium-glucose transport protein-2 inhibitors in patients with eGFR < 60 mL/min/1.73 m².³² Finally, specific recommendations exist for iodinated radiocontrast media administration in patients with GFR < 60 mL/min/1.73 m², whereas the use of oral phosphate-containing bowel preparations should be avoided in people with CKD stage 3a–5.⁴

Our findings confirm that, compared with the CKD-EPI formula, the BIS formula classifies more patients in CKD stage 3a–5; that is, in CKD stages for which specific diagnostic and therapeutic measures are recommended.⁴ Also using CysC will slightly decrease the discrepancy between formulas; the improvement in concordance should be weighted for the cost of measuring cystatin (CysC), which is higher than that of measuring serum creatinine. In any case, the CysC-based improvement in concordance between formulas does not

prevent a notable proportion of relative misclassifications in selected populations, like the very old, women and disabled patients. Interestingly, these are the populations that might benefit the most from a correct diagnosis of CKD. It should also be considered that we studied a broad home-dwelling elderly population with good health status, and a much higher rate of discrepancy is expected in settings such the acute care hospital and long-term care, where factors accounting for discrepancy are highly prevalent. Thus, CysC does not resolve the problem of differences in classificatory properties between the two formulas commonly recognized as the best formulas for older adults.

Limitations of the present study deserve consideration. Indeed, eGFR could not be estimated in 111 out of 939 older participants enrolled in the InChianti study because of the lack of serum creatinine and/or CysC. The excluded patients were more frequently men, and had higher weight compared with patients included in the analysis. We are unable to estimate the impact of this selection bias on the final results. Furthermore, the InChianti population was on average in good health. We cannot exclude that the two formulas are differently sensitive to factors such as dehydration and sarcopenia, which are highly prevalent in older patients with acute or chronic disabling conditions. Thus, further comparative analysis in these kinds of patients seems desirable.

The present study also had some strengths. Indeed, the centralized and standardized serum analyses guarantee for the quality of inherent data. Furthermore, the variety of collected variables allowed for the identification of selected sources of divergence between formulas. Finally, all the probands were Caucasian, and this prevents the confounding effects of different ethnicities on CysC levels.³³

In conclusion, the present findings support the notion that CKD-EPI and BIS equations cannot be considered interchangeable to assess eGFR in an elderly population. Indeed, despite a fair overall concordance, the respective eGFR diverge significantly in the range of GFR corresponding to CKD stages 2–3b, and this might dramatically impact our clinical conduit. Furthermore, in older and disabled people, this divergence is expected to increase. Finally, using creatinine/CysC-based rather than creatinine-based equations marginally improves the concordance between CKD-EPI and BIS. Thus, the observed discrepancy between CKD-EPI and BIS formulas makes a validation study against measured GFR in the frail and multimorbid population highly desirable.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

Bland–Altman plot of the difference between (a) Chronic Kidney Disease Epidemiological Collaboration (CKD-EPI) and (b) Berlin Initiative Study (BIS) equations against the average of the two estimates. Dashed lines represent 95% limits of agreement. BIS_{cre} creatinine-based Berlin Initiative Study equation; BIS_{cre-cys}, creatinine-/cystatin-C-based Berlin Initiative Study equation; CKD-EPI_{cre}, creatinine-based Chronic Kidney Disease Epidemiological Collaboration equation; CKD-EPI_{cre-cys} creatinine-/cystatin-C-based Chronic Kidney Disease Epidemiological Collaboration equation.

Table 1

General characteristics of the participants studied

Age (years)	74.4 ± 6.9
Sex (male)	355 (42.9)
Actual bodyweight (kg)	68.6 ± 12.3
Ideal body weight (kg)	52.5 ± 10.1
Actual bodyweight/ideal bodyweight ratio	1.33 ± 0.24
BMI (kg/m ²)	27.4 ± 4.0
Smoking habits	
Non-smoker	499 (60.3)
Ex-smoker	218 (26.3)
Smoker	111 (13.4)
Hypertension	521 (62.9)
Heart failure	35 (4.2)
Stroke	62 (4.3)
TIA	24 (1.7)
Peripheral arterial disease	97 (11.7)
Chronic liver disease	5 (0.6)
COPD	57 (6.9)
Cancer	50 (6.0)
Dementia	34 (4.1)
Parkinson's disease	6 (0.7)
Hip fracture	21 (2.5)
Metabolic syndrome	197 (23.8)
Diabetes	101 (12.2)
Dysthyroidism	28 (3.4)
Use of systemic steroids	15 (1.8)
No. lost BADL at baseline	0.2 ± 0.7
MMSE score	25.1 ± 3.2
CES-D score	12.8 ± 8.8
Creatinine (mg/dL)	0.92 ± 0.21
Cystatin-C (mg/L)	1.0 ± 0.28
Muscle area ST 66% tibia (mm ³)	6206 ± 1266
Muscle density ST 66% tibia (mg/cm ³)	70.7 ± 3.7
Creatinine-based eGFR (mL/min/1.73 m ²)	
CKD-EPI _{cre}	72.0 ± 13.4
BIS _{cre}	62.5 ± 12.0
Creatinine/cystatin-C-based eGFR (mL/min/1.73 m ²)	
CKD-EPI _{cre-cys}	72.7 ± 16.0
BIS _{cre-cys}	65.3 ± 13.5

n = 828. BADL, basic activities of daily living; BIS_{cre}, creatinine-based Berlin Initiative Study equation; BIS_{cre-cys}, creatinine-/cystatin-C-based Berlin Initiative Study equation; BMI, body mass index; CES-D, Center for Epidemiological

Studies-Depression scale; CKD-EPI_{cre}, creatinine-based Chronic Kidney Disease Epidemiological Collaboration equation; CKD-EPI_{cre-cys}, creatinine-/cystatin-C-based Chronic Kidney Disease Epidemiological Collaboration equation; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; MMSE, Mini-Mental State Examination; TIA, Transient ischemic attack.

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Table 2

Agreement of Chronic Kidney Disease Epidemiological Collaboration and Berlin Initiative Study stratified by age

Age 65–79 years		CKD-EPI _{cre}			κ	<i>P</i>
		90	89.9–60	59.9–45	44.9–30	<30
BIS _{cre}	90	17 (25.0)				0.40 0.001
	89.9–60	51 (75.0)	376 (75.4)			
	59.9–45		123 (24.6)	74 (96.1)		
	44.9–30			3 (3.9)	2 (100)	
	<30					2 (100)
CKD-EPI _{cre-cys}						
BIS _{cre-cys}	90		89.9–60	59.9–45	44.9–30	<30
						κ <i>P</i>
						0.42 0.001
	90	29 (25.2)				
	89.9–60	86 (74.8)	381 (82.5)			
	59.9–45		81 (17.5)	57 (91.9)	1 (14.3)	
	44.9–30			5 (8.1)	6 (85.7)	
	<30					2 (100)
Age 80 years		CKD-EPI _{cre}			κ	<i>P</i>
		90	89.9–60	59.9–45	44.9–30	<30
BIS _{cre}	90					0.23 0.001
			34 (33.3)			
	89.9–60		68 (66.7)	41 (63.1)		
	59.9–45			24 (36.9)		
	44.9–30				9 (100)	
	<30					4 (100)
CKD-EPI _{cre-cys}						
BIS _{cre-cys}	90		89.9–60	59.9–45	44.9–30	<30
						κ <i>P</i>
						0.49 0.001
	90					
	89.9–60					

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Age 65–79 years	CKD-EPI _{cre}					κ	<i>P</i>
	90	89.9–60	59.9–45	44.9–30	<30		
90	2 (25.0)						
89.9–60	6 (75.0)	36 (46.2)					
59.9–45		52 (53.8)	57 (81.4)				
44.9–30			13 (18.6)	16 (100)			
<30					8 (100)		

BIS_{cre}, creatinine-based Berlin Initiative Study equation; BIS_{cre-cys}, creatinine-/cystatin-C-based Berlin Initiative Study equation; CKD-EPI_{cre}, creatinine-based Chronic Kidney Disease Epidemiological Collaboration equation; CKD-EPI_{cre-cys}, creatinine-/cystatin-C-based Chronic Kidney Disease Epidemiological Collaboration equation.

Table 3
Agreement of Chronic Kidney Disease Epidemiological Collaboration and Berlin Initiative Study stratified by sex

Males		CKD-EPI _{cre}			κ	P
		90	89.9–60	59.9–45	44.9–30	<30
BIS _{cre}						0.40 0.001
	90	7 (20.6)				
	89.9–60	27 (79.4)	204 (75.3)			
	59.9–45		67 (24.7)	40 (90.9)		
	44.9–30			4 (9.1)	3 (100)	
	<30					3 (100)
			CKD-EPI _{cre-cys}			
	90		89.9–60	59.9–45	44.9–30	<30
BIS _{cre-cys}						κ P
	90	19 (26.4)				0.48 0.001
	89.9–60	53 (73.6)	182 (81.3)			
	59.9–45		42 (18.8)	45 (91.8)		
	44.9–30			4 (8.2)	6 (100)	
	<30					4 (100)
Females		CKD-EPI _{cre}			κ	P
		90	89.9–60	59.9–45	44.9–30	<30
BIS _{cre}						0.36 0.001
	90	10 (29.4)				
	89.9–60	24 (70.6)	206 (62.4)			
	59.9–45		124 (37.6)	75 (76.5)		
	44.9–30			23 (23.5)	8 (100)	
	<30					3 (100)
			CKD-EPI _{cre-cys}			
	90		89.9–60	59.9–45	44.9–30	<30
BIS _{cre-cys}						κ P
	90					0.48 0.001

Males	CKD-EPI _{cre}				κ	<i>P</i>
	90	89.9–60	59.9–45	44.9–30		
90	12 (23.5)					
89.9–60	39 (76.5)	235 (74.4)				
59.9–45		81 (25.6)	69 (83.1)	1 (5.9)		
44.9–30			14 (16.9)	16 (94.1)		
<30					6 (100)	

BIS_{cre}, creatinine-based Berlin Initiative Study equation; BIS_{cre-cys}, creatinine-/cystatin-C-based Berlin Initiative Study equation; CKD-EPI_{cre}, creatinine-based Chronic Kidney Disease Epidemiological Collaboration equation; CKD-EPI_{cre-cys}, creatinine-/cystatin-C-based Chronic Kidney Disease Epidemiological Collaboration equation.

Agreement of Chronic Kidney Disease Epidemiological Collaboration and Berlin Initiative Study stratified by basic activities of daily living disability

No BADL disability		CKD-EPI _{cre}			κ	P
		90	89.9–60	59.9–45	44.9–30	<30
BIS _{cre}						
	90	16 (24.2)				
	89.9–60	50 (75.8)	401 (68.9)			
	59.9–45		181 (31.1)	112 (83.6)		
	44.9–30			22 (16.4)	7 (100)	
	<30				5 (100)	
CKD-EPI _{cre-cys}						
	90		89.9–60	59.9–45	44.9–30	<30
	89.9–60					
	59.9–45					
	44.9–30					
	<30					
BIS _{cre-cys}						
	90	31 (25.6)				
	89.9–60	90 (74.4)	409 (78.1)			
	59.9–45		115 (21.9)	107 (87.0)	1 (5.3)	
	44.9–30			16 (13.0)	18 (94.7)	
	<30				7 (100)	
Dependency in at least 1 BADL						
		90	89.9–60	59.9–45	44.9–30	<30
BIS _{cre}						
	90	1 (50.0)				
	89.9–60	1 (50.0)	9 (47.4)			
	59.9–45		10 (52.6)	3 (37.5)		
	44.9–30			5 (62.5)	4 (100)	
	<30				1 (100)	
CKD-EPI _{cre-cys}						
	90		89.9–60	59.9–45	44.9–30	<30
BIS _{cre-cys}						

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No BADL disability	CKD-EPI _{cre}					κ	P
	90	89.9–60	59.9–45	44.9–30	<30		
90							
89.9–60	2 (100)	8 (50.0)					
59.9–45		8 (50.0)	7 (77.8)				
44.9–30			2 (22.2)	4 (100)			
<30					3 (100)		

BADL, basic activities of daily living; BIS_{cre}, creatinine-based Berlin Initiative Study equation; BIS_{cre-cys}, creatinine-/cystatin-C-based Berlin Initiative Study equation; CKD-EPI_{cre}, creatinine-based Chronic Kidney Disease Epidemiological Collaboration equation; CKD-EPI_{cre-cys}, creatinine-/cystatin-C-based Chronic Kidney Disease Epidemiological Collaboration equation.