

Journal Homepage: www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/24254
DOI URL: <http://dx.doi.org/10.21474/IJAR01/24254>



RESEARCH ARTICLE

DIAGNOSTIC DISCREPANCY AND STAGING RECLASSIFICATION BETWEEN CYSTATIN C AND CREATININE-BASED EGFR IN SARCOPENIC ADULTS: A CROSS-SECTIONAL STUDY

Humayun Kabir, Atiya A Inamdar and Junaid Muntahi Kabir

Manuscript Info

Manuscript History

Received: 16 July 2026

Final Accepted: 18 August 2026

Published: September 2026

Key words:-

Chronic Kidney Disease, Creatinine,
Cystatin C, Glomerular Filtration Rate,
Reclassification, Sarcopenia.

Abstract

Background: Sarcopenia leads to reduced skeletal muscle mass, causing lower endogenously generated serum creatinine and subsequent overestimation of renal clearance when using creatinine based estimated glomerular filtration rate (eGFR_{cr}). Serum cystatin C, produced at a constant rate by nucleated cells, is largely independent of muscle mass. This study aimed to evaluate the extent of diagnostic discordance and stage reclassification between eGFR_{cr} and cystatin C-based eGFR (eGFR_{cys}) in sarcopenic older adults.

Methods: An analytical cross-sectional study was conducted among 260 sarcopenic patients aged ≥ 60 years recruited from a tertiary-care hospital. Sarcopenia was defined using standard criteria combining reduced handgrip strength and low appendicular skeletal muscle mass index. Serum creatinine and cystatin C were determined. eGFR_{cr}

"© 2026 by the Author(s). Published by IJAR under CC BY 4.0. Unrestricted use allowed with credit to the author."

eGFR_{cys}, and the combined eGFR_{cr-cys} were calculated using the 2021 CKD-EPI equations. Categorical staging concordance was evaluated using weighted kappa (κ_w) and reclassification proportions. Continuous differences were evaluated with Bland-Altman analysis and multivariable regression.

Results: The mean age was 68.4 ± 7.1 years. Mean eGFR_{cr} was significantly higher than eGFR_{cys} (78.6 ± 18.4 vs. 56.2 ± 19.8 mL/min/1.73 m², $p < 0.001$), with a mean overestimation bias of 22.4 mL/min/1.73 m². Overall, 38.5% ($n = 100$) of participants were reclassified to a more severe KDIGO CKD stage when assessed by eGFR_{cys}, with the greatest discordance around the threshold of 60 mL/min/1.73 m². Among individuals categorized as non-CKD (≥ 60 mL/min/1.73 m²) by eGFR_{cr}, 34.6% had covert Stage ≥ 3 CKD on eGFR_{cys}. Lower ASMI ($\beta = -0.42$, $p < 0.001$) and lower handgrip strength ($\beta = -0.31$, $p = 0.002$) were independently associated with wider divergence (eGFR_{cr} - eGFR_{cys}).

Conclusion: Creatinine-based equations markedly overestimate kidney function in sarcopenic adults, obscuring clinically significant chronic kidney disease. Incorporating cystatin C prevents missed CKD diagnoses and allows accurate risk stratification and drug dosing in muscle-depleted populations.

Corresponding Author:-Atiya A Inamdar

Introduction:-

Chronic kidney disease (CKD) and sarcopenia frequently coexist, mutually accelerating functional decline, hospitalization, and mortality in aging populations. (1, 2) Sarcopenia characterized by progressive loss of skeletal muscle quantity, quality, and strength, poses a major physiological challenge to routine biochemical monitoring. (3, 4) The most widespread clinical tool for screening renal clearance, serum creatinine-derived estimated glomerular filtration rate ($eGFR_{cr}$), relies fundamentally on the assumption that endogenous creatinine generation is steady and proportional to standard demographic averages. (5)

Creatinine is an endogenous waste product formed by non-enzymatic conversion of creatine and phosphocreatine in skeletal muscle. (6) In the presence of substantial muscle wasting, daily production of creatinine drops sharply. (7) Consequently, circulating serum creatinine levels remain deceptively low even in the face of progressive nephron loss. (8) This creates a systematic "creatinine blind spot," wherein sarcopenic individuals exhibit falsely elevated $eGFR_{cr}$ values, leading to under detection of CKD stage 3 or worse, delayed nephrology referral, and improper clearance-based dosing of narrow-therapeutic-index medications. (9, 10)

Cystatin C, a 13-kDa non-glycosylated basic protein synthesized by all nucleated cells, is freely filtered by the glomerulus, completely reabsorbed, and catabolized by proximal tubular epithelial cells without tubular secretion. (11) Because its generation is independent of muscle bulk, physical exertion, and dietary meat consumption, cystatin C-based estimated glomerular filtration rate ($eGFR_{cys}$) provides a more objective measure of renal clearance in frail or malnourished populations. (12, 13) Furthermore, the mathematical discrepancy between $eGFR_{cr}$ and $eGFR_{cys}$ has emerged as a potential physiological index reflecting the severity of muscle loss itself. (14, 15)

Despite increasing international consensus emphasizing cystatin C in muscle-wasted cohorts, direct comparative data evaluating the scale of diagnostic discordance and categorical stage shifts within South Asian sarcopenic cohorts remain limited. (16, 17) Therefore, this study was designed to assess the degree of CKD stage reclassification between $eGFR_{cr}$ and $eGFR_{cys}$ and investigate its correlation with physical markers of sarcopenia.

Materials and Methods:-

Study Design and Setting: This observational, analytical cross-sectional study was carried out at a tertiary care teaching hospital from January 2025 to February 2026.

Sample Size Calculation: The required sample size was determined using Cochran's formula: (18)

$$n = \frac{Z_{1-\alpha/2}^2 \cdot p(1-p)}{d^2}$$

Assuming a reclassification proportion (p) of 32% based on prior literature examining altered clearance markers in muscle-wasting states, a two-sided type I error (α) of 0.05 ($Z = 1.96$), and an absolute precision margin (d) of 6% (0.06) (19)

$$n = \frac{(1.96)^2 \times 0.32 \times (1 - 0.32)}{(0.06)^2} \approx 232$$

Accounting for an anticipated 10% rate of non-evaluable tests (e.g., sample hemolysis, incomplete physical assessment), the final target sample size was set at 260 participants. Consecutive systematic sampling from outpatient clinics was utilized.

Study Population:-

Adults aged ≥ 60 years meeting standard diagnostic criteria for confirmed sarcopenia (assessed by low grip strength and reduced appendicular skeletal muscle mass as per Asian Working Group for Sarcopenia - AWGS criteria). (4) Individuals with acute kidney injury within the past 30 days, on current maintenance dialysis, getting active systemic corticosteroid therapy (≥ 20 mg/day prednisone equivalent), uncontrolled thyroid disorders (overt hyper- or hypothyroidism), active malignancy, and severe localized or generalized oedema precluding were excluded from the study. (20, 21)

Clinical & Anthropometric Assessment:-

Sarcopenia was staged according to regional consensus guidelines:-

- **Muscle Strength:** Evaluated using a calibrated Jamar hydraulic hand dynamometer. Three trials were performed on each hand, and the maximal reading was recorded (< 28 kg for men, < 18 kg for women). (4)

- **Muscle Mass:** Assessed by multi-frequency bioelectrical impedance analysis (BIA) performed under fasting conditions with an empty bladder. Appendicular Skeletal Muscle Mass Index ($ASMI = ASM/height^2$) was determined, with cut-offs set at $< 7.0 \text{ kg/m}^2$ in men and $< 5.7 \text{ kg/m}^2$ in women. (4)

Laboratory Procedures & Calculations: Venous blood samples were collected between 08:00 and 10:00 AM after an overnight fast.

- Serum creatinine was quantified using an enzymatic method traceable to isotope dilution mass spectrometry (IDMS)(22)
- Serum cystatin C was measured using particle-enhanced immunoturbidimetry calibrated against ERM-DA471/IFCC reference materials. (23)

GFR calculations utilized the 2021 CKD-EPI equations without race adjustment: (24):-

- $eGFR_{cr}$ (2021 CKD-EPI Creatinine) (24)
- $eGFR_{cys}$ (2012 CKD-EPI Cystatin C) (12)
- $eGFR_{cr-cys}$ (2021 CKD-EPI Creatinine–Cystatin C) (24)

CKD stages were designated following KDIGO definitions: Stage 1 (≥ 90), Stage 2 (60--89), Stage 3a (45--59), Stage 3b (30--44), Stage 4 (15--29), and Stage 5 ($< 15 \text{ mL/min/1.73 m}^2$). (25)

Statistical Analysis:-

Analyses were completed using IBM SPSS Statistics version 26.0 and R version 4.3. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (interquartile range, IQR) according to distribution normality assessed via the Shapiro-Wilk test. Differences between paired $eGFR$ values were analyzed using the Wilcoxon signed-rank test or paired t-test. Categorical agreement across CKD stages was evaluated using quadratic weighted kappa (κ_w). (26) Concordance and discordant shifts were evaluated via the McNemar-Bowker test of symmetry. Multivariable linear regression was performed to evaluate predictors of the $eGFR$ discrepancy ($\Delta eGFR = eGFR_{cr} - eGFR_{cys}$). A two-tailed p-value < 0.05 was considered statistically significant.

Ethical Considerations:-

The study protocol received institutional review board approval. All participants or their legal representatives provided written informed consent in accordance with the Declaration of Helsinki.

Results:-

A total of 260 sarcopenic older adults were evaluated, and the mean age of the participants was 68.4 ± 7.1 years; 158 (60.8%) were men and 102 (39.2%) were women. Hypertension was present in 164 (63.1%) and type 2 diabetes mellitus in 118 (45.4%).

Baseline Parameters and Renal Metrics:-

The mean serum creatinine was $0.98 \pm 0.31 \text{ mg/dL}$, while mean serum cystatin C was $1.34 \pm 0.44 \text{ mg/L}$. Mean $eGFR_{cr}$ was significantly higher than $eGFR_{cys}$ (78.6 ± 18.4 vs. $56.2 \pm 19.8 \text{ mL/min/1.73 m}^2$, paired difference $22.4 \pm 11.2 \text{ mL/min/1.73 m}^2$, $p < 0.001$).

Bold diagonal values indicate exact agreement ($n = 134, 51.5\%$). Weighted kappa $\kappa_w = 0.44$ (95% CI: 0.37--0.51), indicating moderate agreement. (Figure 1) Downward reclassification (worse stage by $eGFR_{cys}$) occurred in 118 patients (45.4%). McNemar-Bowker test $p < 0.001$.

Staging Discrepancy Around the $60 \text{ mL/min/1.73 m}^2$ Threshold (Table 1 & Figure 1)

When evaluating the standard clinical threshold for CKD ($< 60 \text{ mL/min/1.73 m}^2$):-

1. Based on $eGFR_{cr}$, only 74 patients (28.5%) were identified as having CKD Stage ≥ 3 .
2. Based on $eGFR_{cys}$, 139 patients (53.5%) had an $eGFR < 60 \text{ mL/min/1.73 m}^2$.
3. Among 186 participants classified as non-CKD (Stages 1 and 2) by creatinine, 65 (34.9%) were reclassified to Stage ≥ 3 CKD upon measuring cystatin C.

The primary driver of the eGFR discrepancy was skeletal muscle quantity, as reflected by the Appendicular Skeletal Muscle Mass Index (ASMI). ASMI exhibited the strongest independent inverse association with the eGFR gap (unstandardized $\beta = -3.45$, standardized $\beta = -0.42$, $t = -5.94$, $p < 0.001$). This indicates that for every 1 kg/m² reduction in appendicular muscle mass, the creatinine-based overestimation of kidney function widened by 3.45 mL/min/1.73 m². Muscle quality and function showed a congruent pattern: handgrip strength was also an independent negative predictor ($\beta = -0.38$, standardized $\beta = -0.31$, $t = -3.16$, $p = 0.002$), demonstrating that progressive physical weakness independently amplifies the gap between creatinine- and cystatin C-based clearance estimates. (Table 2)

Among demographic and biochemical covariates, advancing age displayed a modest, statistically significant positive association with the discrepancy gap ($\beta = 0.18$, standardized $\beta = 0.12$, $t = 2.25$, $p = 0.025$), indicating greater overestimation of renal clearance in older individuals even after controlling for body composition. In contrast, male sex ($\beta = 2.14$, $p = 0.071$) and baseline serum albumin ($\beta = -1.82$, $p = 0.084$) trended toward wider and narrower discrepancies respectively, but neither reached statistical significance in the fully adjusted model. Collectively, these results confirm that the discordance between the two equations is directly proportional to the anatomical and functional severity of sarcopenia. Lastly, the overall model was statistically significant ($F = 31.4$, $p < 0.001$) and demonstrated robust explanatory power, accounting for 38.2% of the total variance in the divergence between the two filtration markers ($R^2 = 0.382$, Adjusted $R^2 = 0.369$).

Table 1: Cross-Classification Matrix of CKD Staging by eGFR_{cr} vs. eGFR_{cys} (N = 260)

CKD Stage by eGFR _{cr}	CKD Stage by eGFR _{cys}						Total by eGFR _{cr}
	Stage 1 (≥90)	Stage 2 (60–89)	Stage 3a (45–59)	Stage 3b (30–44)	Stage 4 (15–29)	Stage 5 (<15)	
Stage 1 (≥ 90)	22	31	5	0	0	0	58
Stage 2 (60--89)	0	68	46	14	0	0	128
Stage 3a (45--59)	0	0	23	18	2	0	43
Stage 3b (30--44)	0	0	0	14	8	0	22
Stage 4 (15--29)	0	0	0	0	6	2	8
Stage 5 (< 15)	0	0	0	0	0	1	1
Total by eGFR_{cys}	22	99	74	46	16	3	260

Table 2: Multivariable Linear Regression Predicting the Discrepancy Gap ($\Delta eGFR = eGFR_{cr} - eGFR_{cys}$) (N = 260)

Independent Predictor	Unstandardized β	Standard Error	Standardized β	t-statistic	p-value
Constant	44.82	6.12	—	7.32	< 0.001
Age (Years)	0.18	0.08	0.12	2.25	0.025
Sex (Male = 1, Female = 0)	2.14	1.18	0.09	1.81	0.071
ASMI (kg/m ²)	-3.45	0.58	-0.42	-5.94	< 0.001
Handgrip Strength (kg)	-0.38	0.12	-0.31	-3.16	0.002
Serum Albumin (g/dL)	-1.82	1.05	-0.08	-1.73	0.084
Dependent variable: eGFR _{diff} (mL/min/1.73 m ²). Model statistics: $R^2 = 0.382$, Adjusted $R^2 = 0.369$, $F = 31.4$, $p < 0.001$.					

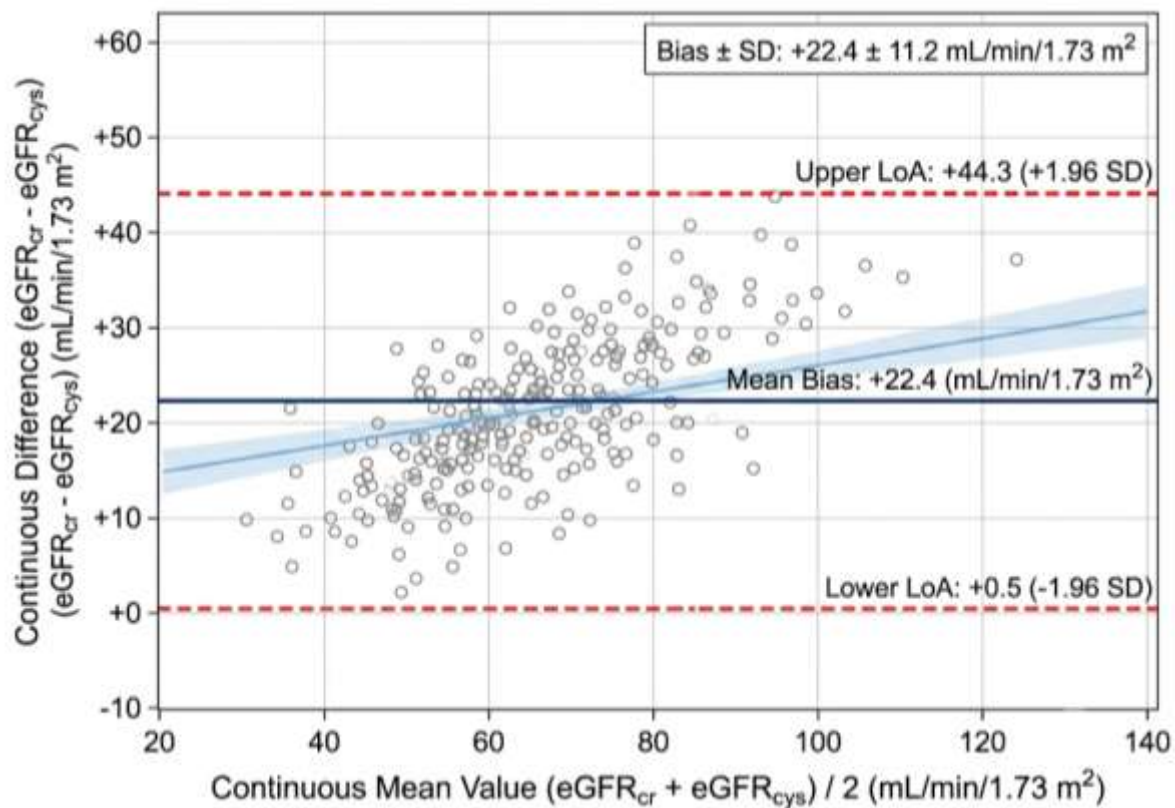


Figure 1: Bland–Altman Plot Illustrating the Disagreement Between Creatinine- and Cystatin C–Based eGFR in Sarcopenic Adults (N = 260)

Discussion:-

In this cross-sectional study of sarcopenic older adults, reliance on creatinine-based equations introduced a substantial overestimation bias in renal clearance, resulting in misclassification of over one-third of the study cohort. When evaluated with cystatin C, more than half of the participants had GFR values consistent with Stage 3 to 5 CKD, compared to fewer than thirty percent by creatinine alone.

The observed mean overestimation bias of $22.4 \text{ mL/min/1.73 m}^2$ directly reflects the pathophysiological reduction of muscle-derived creatinine synthesis. Because the 2021 CKD-EPI creatinine equation assumes standard muscle mass for a given age and sex (24), low circulating creatinine is interpreted as hyper-efficient renal clearance. This physiological bias is consistent with findings reported by Inker et al. (24) and Levey et al. (12), who noted that non-GFR determinants of serum creatinine led to systematic overestimation of GFR in individuals with low body mass index and muscle wasting. Similar magnitude differences were observed by Baxmann et al. (6), who demonstrated that muscle mass explains up to 50% of the variance in serum creatinine concentrations, whereas serum cystatin C concentrations remain unaffected by muscle cross-sectional area.

When compared with prior investigations in geriatric cohorts, our findings closely parallel the work of Purde et al. (27) and Kilbride et al. (28), who demonstrated that eGFR_{cr} routinely overestimates measured GFR in frail, community-dwelling octogenarians. Kilbride et al. (28) reported that creatinine-based formulas overestimated measured clearance by an average of 15 to $20 \text{ mL/min/1.73 m}^2$ when compared against iohexol clearance. However, while Kilbride et al. (28) studied an unselected elderly population, our study specifically enrolled individuals with confirmed sarcopenia diagnosed via bioimpedance and dynamometry, which explains the even larger mean overestimation ($22.4 \text{ mL/min/1.73 m}^2$) observed in our cohort. In contrast, in healthy adult populations with preserved muscle mass evaluated by Rule et al. (29), creatinine-based formulas show minimal bias relative to cystatin C, highlighting that the marked divergence between the two markers is specific to states of reduced muscularity.

The categorical reclassification observed in our study (38.5% to a more severe stage, and 34.9% covert CKD unmasked among those with $eGFR_{cr} \geq 60 \text{ mL/min/1.73 m}^2$) is substantially higher than the reclassification rates documented in general CKD screening cohorts. For instance, Shlipak et al. (30) evaluated large population-based cohorts and observed that measuring cystatin C reclassified approximately 13% of participants across the $60 \text{ mL/min/1.73 m}^2$ threshold. The markedly higher rate of downward reclassification in our study underscores that general population estimates cannot be extrapolated to sarcopenic individuals, where the "creatinine blind spot" is far more pronounced. Our findings also corroborate studies in end-stage liver disease by Mindikoglu et al. (31) and cirrhotic cohorts by Piano et al. (32), who noted that profound muscle sarcopenia masked renal impairment in over 40% of patients when relying on standard creatinine-based formulas, whereas cystatin C accurately identified true renal clearance verified by measured isotopic GFR.

The distortion identified around the critical threshold of $60 \text{ mL/min/1.73 m}^2$ carries profound clinical ramifications. In geriatric medicine, dosing for narrow-therapeutic-index drugs cleared primarily by the kidneys, such as direct oral anticoagulants (DOACs), gabapentin, SGLT2 inhibitors, and hydrophilic antibiotics, is determined by renal clearance cut-offs at 60, 45, or $30 \text{ mL/min/1.73 m}^2$ (33, 34). As emphasized by Corsonello et al. (35), overestimating GFR in frail older patients leads directly to inappropriate drug dosing, increased adverse drug reactions, and preventable hospital admissions. Relying on $eGFR_{cr}$ in sarcopenic individuals risks drug accumulation toxicity while simultaneously delaying nephrology interventions, dietary protein modifications, and cardiovascular risk factor optimization (36).

Multivariable linear regression confirmed that lower ASMI and lower handgrip strength were independent drivers of the divergence between the two markers ($\Delta eGFR$). This inverse association aligns directly with the conceptual framework proposed by Kashani et al. (14) and validated by Kim et al. (37), who established the creatinine-to-cystatin C ratio as the "Sarcopenia Index." While those investigators used the ratio to estimate muscle mass, our findings demonstrate the reverse clinical reality: physical muscle wasting directly drives mathematical divergence between the two $eGFR$ equations ($\beta = -3.45$ for ASMI and $\beta = -0.38$ for grip strength). This confirms that the discrepancy gap itself acts as an objective physiological biomarker of muscular depletion.

Strengths and Limitations:-

Key strengths of this study include the standardized, simultaneous evaluation of muscle quality and mass using validated diagnostic criteria (multi-frequency BIA and calibrated Jamar dynamometry) combined with IDMS-traceable creatinine and IFCC-standardized cystatin C assays. However, several limitations must be acknowledged. First, measured GFR (mGFR) using exogenous clearance markers such as iohexol or inulin was not performed due to institutional resource constraints. Nonetheless, extensive multicenter validation by Inker et al. (24) and Stevens et al. (38) has robustly validated the superior accuracy of $eGFR_{cys}$ against mGFR in patients with altered body habitus. Second, the single-center cross-sectional design precludes assessment of longitudinal renal progression, cardiovascular events, or mortality. Third, non-GFR determinants of cystatin C, such as subclinical inflammation or adiposity, could introduce minor confounding (39); however, strict protocol exclusion of patients with active systemic infections, thyroid dysfunction, and systemic corticosteroid therapy minimized these confounders.

Conclusion:-

Serum creatinine systematically overestimates glomerular filtration in sarcopenic older adults, masking Stage ≥ 3 chronic kidney disease in over one-third of affected individuals. Incorporating cystatin C provides a more accurate reflection of renal status in patients with documented muscle wasting. In geriatric and cachectic populations, clinical guidelines should prioritize $eGFR_{cys}$ or the combined $eGFR_{cr-cys}$ equation to ensure accurate staging, safe pharmacotherapy, and timely clinical intervention.

References:-

1. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet*. 2019;393(10191):2636–46.
2. Moorthi RN, Avin KG. Clinical approach to muscle wasting in chronic kidney disease. *Semin Nephrol*. 2017;37(2):128–38.
3. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):16–31.

4. Chen LK, Woo J, Assantachai P, Arai H, Liang CK, Won CW, et al. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc.* 2020;21(3):300–7.e2.
5. Levey AS, Inker LA, Coresh J. GFR evaluation: as a marker of kidney function and a risk factor for challenges and solutions. *J Am Soc Nephrol.* 2014;25(11):2340–51.
6. Baxmann AC, Ahmed MS, Marques NC, Menon VB, Pereira AB, Kirsztajn GM, et al. Influence of muscle mass and physical activity on serum creatinine levels. *Clin J Am Soc Nephrol.* 2008;3(2):348–54.
7. Heymsfield SB, Arteaga C, McManus C, Smith J, Moffitt S. Measurement of muscle mass in humans: validity of the 24-hour urinary creatinine method. *Am J Clin Nutr.* 1983;37(3):478–94.
8. Perrone RD, Madias NE, Levey AS. Serum creatinine as an index of renal function: new insights into old concepts. *Clin Chem.* 1992;38(10):1933–53.
9. Musso CG, Álvarez-Gregori J, Jauregui J, Macías-Núñez JF. The dilemma of estimating renal function in elderly patients: which formula to use? *Int Urol Nephrol.* 2012;44(3):981–4.
10. Dowling TC, Wang LM, Shenasa M. Discrepancies in estimated glomerular filtration rate equations for drug dosing in hospitalized geriatric patients. *Pharmacotherapy.* 2013;33(10):1033–40.
11. Filler G, Bökenkamp A, Hofmann W, Le Bricon T, Martínez-Brú C, Grubb A. Cystatin C as a marker of GFR—history, indications, and future research. *Clin Biochem.* 2005;38(1):1–8.
12. Inker LA, Schmid CH, Tighiouart H, Eckfeldt JH, Feldman HI, Greene T, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med.* 2012;367(1):20–9.
13. Shlipak MG, Mates R, Peralta CA. Update on cystatin C: incorporation into clinical practice. *Am J Kidney Dis.* 2013;62(3):595–603.
14. Kashani K, Frazee EN, Kukrálová L, Sarvottam K, Herasevich V, Kashyap R, et al. Evaluating muscle mass by using markers of kidney function: development of the sarcopenia index. *Crit Care Med.* 2017;45(1):e23–9.
15. Tabara Y, Kohara K, Okada Y, Ohyagi Y, Igase M. Creatinine-to-cystatin C ratio as a marker of skeletal muscle mass in older adults: J-SHIPP study. *Clin Nutr.* 2020;39(6):1857–62.
16. Singh AK, Farag YM, Mittal BV, Subramanian KK, Reddy SR, Acharya VN, et al. Epidemiology and risk factors of chronic kidney disease in India—results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. *BMC Nephrol.* 2013;14:114.
17. Shriram V, Mahadevan S, Subitha L, Balasubramaniyan V, Jagadeeshwaran AM, Govindaraj V. Sarcopenia among elderly in rural South India: a community-based cross-sectional study. *J Frailty Sarcopenia Falls.* 2021;6(2):49–56.
18. Cochran WG. *Sampling Techniques.* 3rd ed. New York: John Wiley & Sons; 1977.
19. Pöge U, Gerhardt T, Stoffel-Wagner B, Klehr HU, Sauerbruch T, Woitas RP. Calculation of glomerular filtration rate based on cystatin C in cirrhotic patients. *Nephrol Dial Transplant.* 2006;21(3):660–4.
20. Fricker M, Wiesli P, Brändle M, Schwegler B, Schmid C. Impact of thyroid dysfunction on serum cystatin C. *Kidney Int.* 2003;63(5):1944–7.
21. Risch L, Herklotz R, Blumberg A, Huber AR. Effects of glucocorticoid immunosuppression on serum cystatin C concentrations in renal transplant patients. *Clin Chem.* 2001;47(11):2055–9.
22. Myers GL, Miller WG, Coresh J, Fleming J, Greenberg N, Greene T, et al. Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clin Chem.* 2006;52(1):5–18.
23. Grubb A, Blirup-Jensen S, Lindström V, Schmidt C, Althaus H, Zegers I. First certified reference material for cystatin C in human serum: ERM-DA471/IFCC. *Clin Chem Lab Med.* 2010;48(11):1619–21.
24. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med.* 2021;385(19):1737–49.
25. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl.* 2013;3(1):1–150.
26. Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. *Psychol Bull.* 1968;70(4):213–20.
27. Purde MT, Nock S, Risch L, Medina-Escobar L, Grebhardt C, Nydegger UE, et al. The cystatin C-based CKD-EPI equation performs better than creatinine-based formulas in elderly hospitalized patients. *Clin Nephrol.* 2016;85(4):216–24.
28. Kilbride HS, Stevens PE, Eaglestone G, Knight S, Carter JL, Delaney MP, et al. Accuracy of the MDRD (Modification of Diet in Renal Disease) study and CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equations for estimation of GFR in the elderly. *Am J Kidney Dis.* 2013;61(1):57–66.
29. Rule AD, Teo BW. GFR estimation in healthy populations: should we use creatinine, cystatin C, or both? *Nephrol Dial Transplant.* 2014;29(8):1462–4.

30. Shlipak MG, Matsushita K, Ärnlöv J, Inker LA, Woodward M, de Jong PE, et al. Cystatin C versus creatinine in determining risk based on kidney function. *N Engl J Med.* 2013;369(10):932–43.
31. Mindikoglu AL, Dowling TC, Weir MR, Seliger SL, Christenson RH, Magder LS. Performance of chronic kidney disease epidemiology collaboration creatinine-cystatin C equation for estimating glomerular filtration rate in patients with cirrhosis. *Hepatology.* 2014;59(4):1532–42.
32. Piano S, Rosi S, Maresio G, Fasolato S, Cavallin M, Romano A, et al. Evaluation of the CKD-EPI equation estimating glomerular filtration rate with cystatin C in patients with cirrhosis. *Clin Chem Lab Med.* 2014;52(12):e271–4.
33. Helldén A, Odar-Cederlöf I, Nilsson G, Sjövikar S, Söderström A, von Euler M, et al. Renal function estimations and dose recommendations for direct oral anticoagulants in frail elderly patients. *Eur J Clin Pharmacol.* 2020;76(11):1537–44.
34. Stevens LA, Nolin TD, Richardson MM, Feldman HI, Lewis JB, Rodby R, et al. Comparison of drug dosing recommendations based on measured GFR and kidney function estimating equations. *Am J Kidney Dis.* 2009;54(1):33–42.
35. Corsonello A, Pedone C, Corica F, Mussi C, Carbonin P, Incalzi RA. Concealed renal failure and adverse drug reactions in older patients with normal serum creatinine. *Arch Intern Med.* 2005;165(7):790–5.
36. Hallan SI, Ritz E, Lydersen S, Romundstad S, Kvenild K, Orth SR. Combining GFR and albuminuria to classify CKD improves prediction of ESRD. *J Am Soc Nephrol.* 2009;20(5):1069–77.
37. Kim SW, Yoon JS, Won KC, Lee HW. Sarcopenia index using serum creatinine and cystatin C is useful for assessing muscle mass and sarcopenia in patients with type 2 diabetes. *J Diabetes Investig.* 2021;12(11):2039–47.
38. Stevens LA, Coresh J, Schmid CH, Feldman HI, Froissart M, Kusek J, et al. Estimating GFR using serum cystatin C alone and in combination with serum creatinine: a pooled analysis of 3,418 individuals with CKD. *Am J Kidney Dis.* 2008;51(3):395–406.
39. Stevens LA, Schmid CH, Greene T, Li L, Beck GJ, Joffe MM, et al. Factors other than glomerular filtration rate affect serum cystatin C levels. *Kidney Int.* 2009;75(6):652–60.