PREDICTIVE PERFORMANCE OF GLOMERULAR FILTRATION RATE EQUATIONS BASED ON CYSTATIN C, CREATININE AND THEIR COMBINATION IN CRITICALLY ILL PATIENTS

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Background and Importance

- Serum creatinine (SCr) is the most frequently used subrogated parameter to estimate Glomerular Filtration Rate (GFR), however, Cystatin-C (CystC) may reflect GFR changes earlier than SCr.

Aim and Objectives

- To assess the performance of equations based on SCr, CystC, and their combination (SCr-CystC) for estimating GFR in critically ill patients in comparison to 24h-ClCr.

Materials and Methods

- Retrospective, observational study in a tertiary-care hospital (May 2020-July 2022).

- Inclusion criteria: Critically ill patients with CystC, SCr and 24h-ClCr measurements within ± 2 days. Altered thyroid status and corticosteroids use within the previous 5 days were recorded.

- **24h-ClCr** was the **reference method**. GFR was estimated using
  - **SCr**-based equations: CKD-EPI-Cr and Cockcroft-Gault (CG)
  - **Cyst C**-based equations: CKD-EPI-CystC and CAPA
  - **SCr-Cyst C**-based equations: CKD-EPI-Cr-CystC

- Pearson´s correlation coefficients (r^2), concordance correlation coefficients (CCC), bias (difference between estimated GFR and 24h-ClCr) and precision (SD of bias) were calculated. Bland-Altman plots were used to compare GFR estimations with 24h-ClCr.

- Analysis was performed with stratified data: 24h-CrCl <60mL/min/1.73m^2, 60-130mL/min/1.73m^2 and ≥130 mL/min/1.73m^2.

Results

Table 1. Patients' characteristics (n=275)

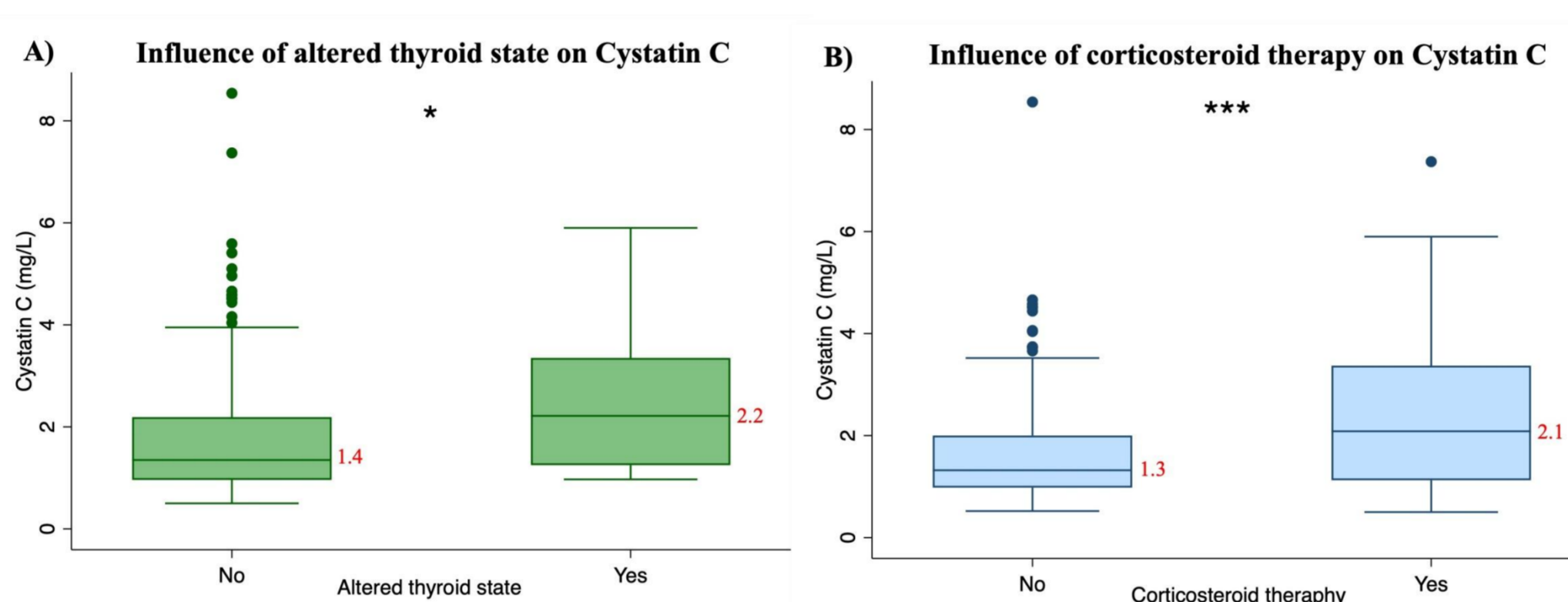| Variable	N
Age (years), mean ± SD	61.2 ± 13.8
Male sex, (%)	176 (64.0)
Caucasian, (%)	266 (96.7)
Weight (kg), mean ± SD	75.7 ± 16.9
Serum creatinine (mg/dL), mean ± SD	1.3 ± 1.1
Serum cystatin C (mg/L), mean ± SD	1.8 ± 1.2
Measured ClCr 24h (mL/min), mean ± SD	77.0 ± 57.7
Measurements with altered thyroid state, (%)	22 (8.0)
Measurements with corticosteroid therapy, (%)	64 (23.3)

Figure 1. Box plot of the influence of thyroid alteration **(A)** and corticosteroid therapy on Cystatin C **(B)**. *p-value < 0.05, **p-value < 0.01, ***p-value < 0.001

Table 2. Performance of creatinine, cystatin C and their combination. (n=275 measurements, 186 patients). CCC: Concordance correlation coefficient

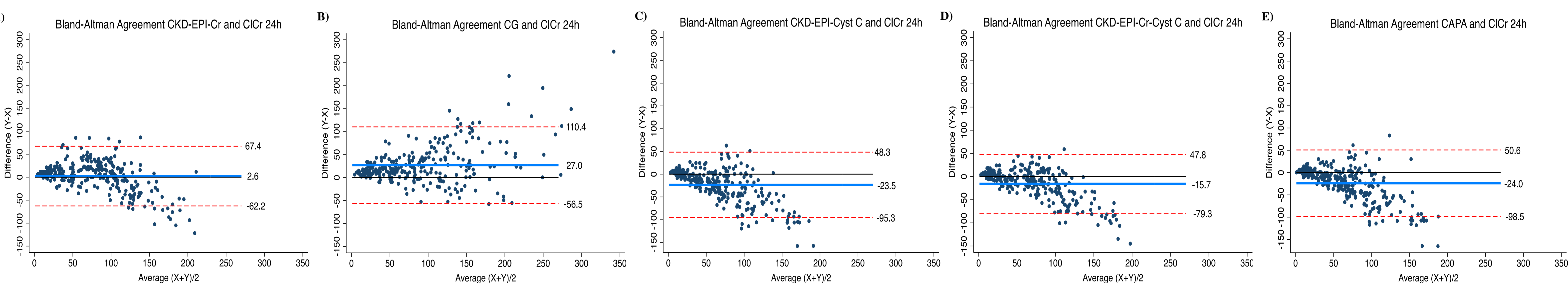| Equation	GFR estimates (Mean±SD mL/min/1.73 m^2)	Bias	Precision	CCC	Cases out of limits (%)
ClCr 24h	77.1 ± 57.7	NA	NA	NA	NA
CKD-EPI-Cr	79.6 ± 42.2	2.56	33.1	0.785	20
CG	104.0 ± 74.0	27.0	42.6	0.734	13
CKD-EPI-Cyst C	53.6 ± 33.6	-23.5	36.6	0.622	16
CKD-EPI-Cr-Cyst C	61.3 ± 35.7	-15.7	32.4	0.732	17
CAPA	53.1 ± 32.6	-24.0	38.0	0.593	19

Figure 2. Bland-Altman plots showing mean differences between estimated GFR and measured ClCr 24h. On the x-axis, the average of the estimated GFR and ClCr 24h is given and on y-axis, the difference between the estimated GFR and ClCr 24h in mL/min. The estimated GFR derived from derived from CKD-EPI-Cr **(A)**, CG **(B)**, CAPA **(C)**, CKD-EPI-Cyst C **(D)**, and CKD-EPI-Cr-Cyst C **(E)** is given. The mean of the differences (solid blue line) and the 95% limits of agreement of the mean differences (red dotted lines), calculated using Bland-Altman plots are displayed.
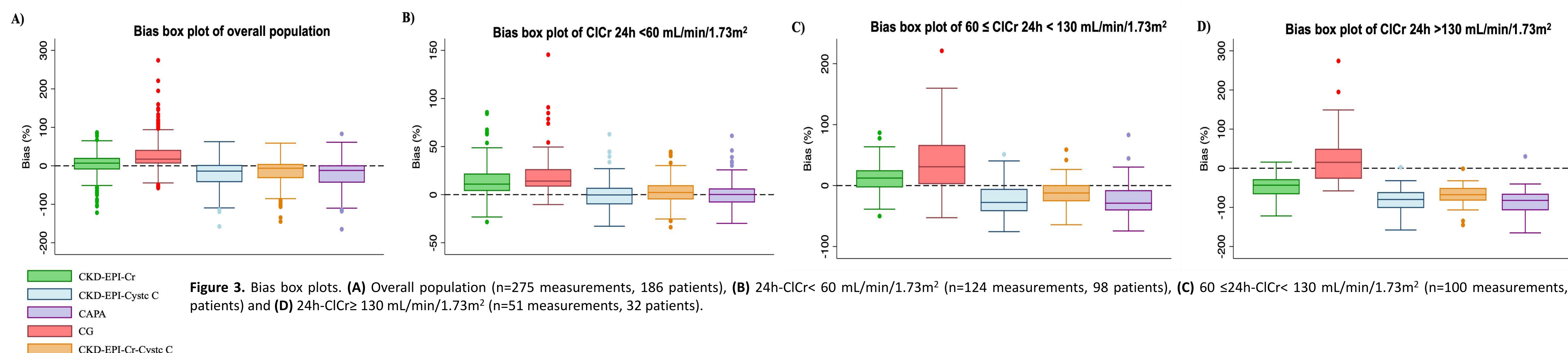
Figure 3. Bias box plots. **(A)** Overall population (n=275 measurements, 186 patients), **(B)** 24h-ClCr< 60 mL/min/1.73m^2 (n=124 measurements, 98 patients), **(C)** 60 ≤24h-ClCr< 130 mL/min/1.73m^2 (n=100 measurements, 71 patients) and **(D)** 24h-ClCr≥ 130 mL/min/1.73m^2 (n=51 measurements, 32 patients).

Legend: CKD-EPI-Cr, CKD-EPI-Cyst C, CAPA, CG, CKD-EPI-Cr-Cyst C

Conclusion and Relevance

- Our study showed no evidence of superiority of any equation over others for all evaluated parameters.
- **Cyst C-based equations** were less biased in individuals with impaired renal function (GFR<60 mL/min/1.73m^2), **CKD-EPI-Cr-Cyst C** performed properly in GFR from 60-130mL/min/1.73m^2 and **CG** in patients >130 mL/min/1.73m^2.