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Refining Pre-Donation Screening Through Creatinine–Cystatin C Co-measurement: From GFR Accuracy to Prognostic Discordance

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Objectives : In living kidney donor evaluation, glomerular filtration rate (eGFR) is typically estimated before proceeding to resource-intensive measured GFR (mGFR). However, creatinine-based eGFR alone may misclassify donor eligibility, particularly when cystatin C levels diverge — a phenomenon termed eGFR discordance. We hypothesized that this discordance reflects underlying physiological difference, with dual implications for accurate donor screening and post-donation renal risk stratification.

Methods : We conducted a retrospective study of donor candidates who underwent simultaneous measurement of serum creatinine, cystatin C, and mGFR (⁹⁹mTc-DTPA clearance). We compared five eGFR equations — CKD-EPIcr (2009), CKD-EPIcys (2012), CKD-EPIcr (2021), CKD-EPIcr–cys (2021), and EKFCcr (2021) against mGFR with misclassification rate at the eligibility threshold of 90 mL/min/1.73 m². We then examined the association between magnitude and direction of cystatin C over creatinine-based eGFR discordance and post-donation acute kidney disease (AKD) with model performance assessed by using calibration plots.

Results : Of 4,854 donor candidates, 1,405 were included (mean age 50.1 years; 45.8% male; mean BMI 24.5 kg/m²), the CKD-EPIcr–cys (2021) equation showed the best agreement with mGFR (Pearson $r = 0.623$, RMSE 17.7, P10 50.5%, P30 96.5%) with highest concordance across all age and sex subgroups. This equation had the lowest total misclassification rate (17.2%) and smallest mean absolute classified discordance (0.710). In addition, a greater positive discrepancy of eGFR was independently associated with lower odds of post-donation AKD (adjusted OR 0.68, 95% CI 0.57–0.81), with calibration plots confirming the robust predictive agreement.

Conclusions : CKD-EPIcr–cys (2021) equation most accurately reflected mGFR, minimizing donor eligibility misclassification before confirmatory testing. Beyond accuracy, the discordance between its constituent biomarkers proves a physiologically meaningful signal — independently predicting post-donation AKD risk. These findings support routine co-measurement of creatinine and cystatin C as a standard component of pre-donation workup.

Table2.jpg



Table 2. Accuracy and Agreement of GFR Estimation Equations Against Measured GFR

Method	Pearson	Spearman	CCC	Bias	RMSE	P30	P10
2009 CKD-EPI _{cr}	0.560	0.591	0.397	-12.14	20.46	94.3	42.4
2012 CKD-EPI _{cys}	0.565	0.572	0.492	-7.94	18.53	95.3	48.4
2021 CKD-EPI _{cr}	0.554	0.588	0.434	-8.28	18.47	95.5	47.3
2021 CKD-EPI _{cr-cys}	0.623	0.639	0.517	-8.41	17.67	96.5	50.5
2021 EKFC _{cr}	0.572	0.594	0.334	-16.64	23.26	92.2	32.0

Pearson and Spearman correlation coefficients, concordance correlation coefficient (CCC), bias, root mean square error (RMSE), and the proportions of estimates within 30% (P30) and 10% (P10) of measured GFR were calculated for each estimated GFR (eGFR) equation.

Abbreviations: CCC, concordance correlation coefficient; RMSE, root mean square error; P30, percentage of eGFR within 30% of measured GFR; P10, percentage of eGFR within 10% of measured GFR; eGFR, estimated glomerular filtration rate; mGFR, measured glomerular filtration rate; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; EKFC, European Kidney Function Consortium; cr, creatinine; cys, cystatin C.

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