Bias and Precision of NMR-Based GFR Estimating Equation in Kidney Transplant Recipients

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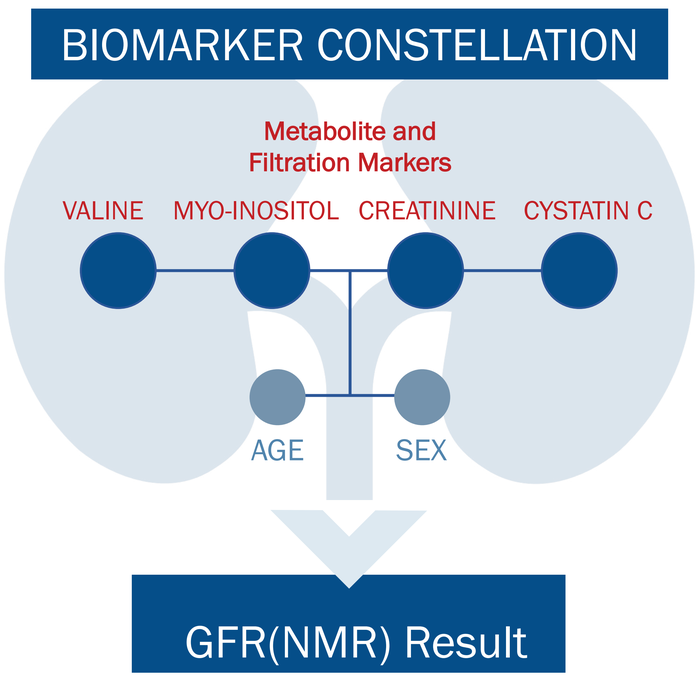
BACKGROUND

An accurate and reliable measurement of glomerular filtration rate (GFR) is essential to monitor for rejection and disease progression post-kidney transplantation. Measured GFR (mGFR) is the current gold standard. However, it has scarce availability at many centers and is labor-intensive. Newer estimated GFR (eGFR) methods containing cystatin C and/or other biomarkers have not been clinically validated in a post-transplant cohort. Here, we evaluated a new NMR-based GFR equation, the GFR_{NMR} that includes serum creatinine, cystatin C, myo-inositol and valine (Fig. 1), following kidney transplantation in a routine clinical setting.

METHODS

Venipuncture for serum collection was performed immediately before mGFR measurement with urinary iothalamate clearance in 67 post-kidney transplant recipients. Serum was stored at 4°C and measured by NMR no later than four days after collection. eGFR was assessed using the following three equations: GFR(NMR); CKD-EPI_{2021}Cr (creatinine); and CKD-EPI_{2021}CrCys (creatinine and cystatin C).

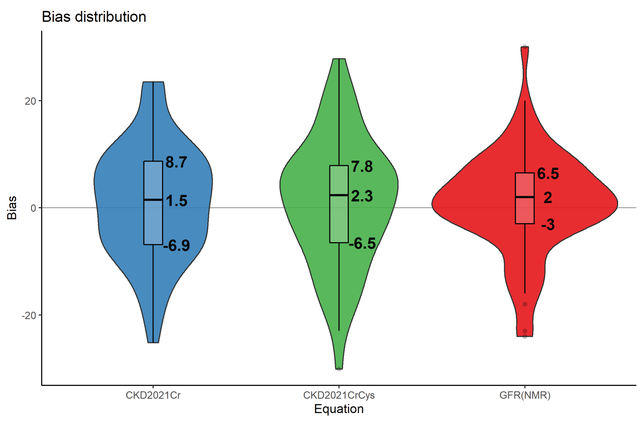
Figure 1. GFR(NMR) Constellation



Bias was calculated as eGFR less mGFR for all equations. The bootstrap method was employed to assess pairwise significance levels between bias distributions interquartile ranges (IQR), and p-value correction was determined with the Benjamini & Hochberg method. Precision, defined as percentage of samples within ±30% and ±15% from the mGFR value (P30 and P15, respectively), was calculated for each equation. Pairwise comparisons were made using McNemar's chi-square and Benjamini & Hochberg correction. Precision was defined as the proportion of eGFR values concordant with mGFR values by CKD clinical stage.

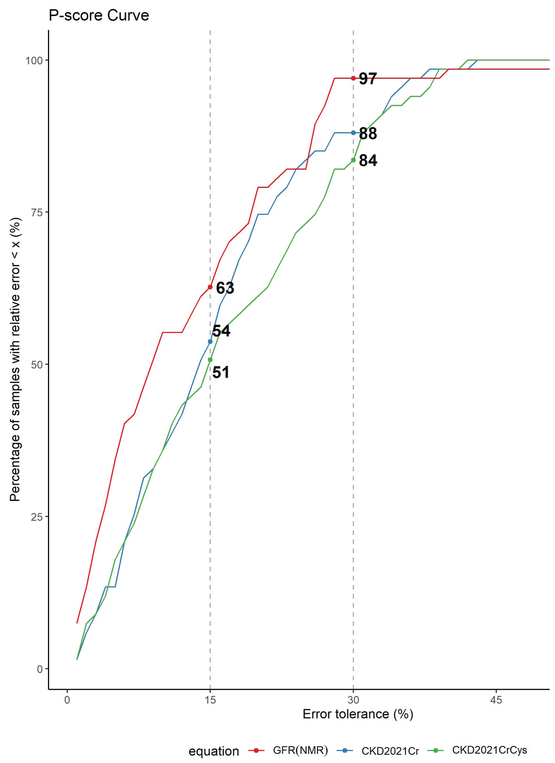
RESULTS

Figure 2. Bias Distribution (mL/min/1.73m²)



P30 for GFR_{NMR} was significantly higher than CKD-EPI_{2021} Cr,Cys (97% vs. 84%, p<0.01) and higher than CKD-EPI_{2021}Cr (88%, p=0.08), (Fig. 2). Similarly, P15 for GFR_{NMR} was 63%, which is higher than the CKD-EPI_{2021}Cr (54%, p=0.35) and CKD-EPI_{2021}CrCys (51%, p=0.19), (Fig. 2).

Figure 3. Precision P-Score Curve



Bias IQR for GFR_{NMR} was 9.5 mL/min/1.73m² (median bias 2.0 mL/min/1.73m²). This is significantly smaller than CKD-EPI_{2021}Cr (bias IQR 15.55 mL/min/1.73m², p<0.05; median bias 1.47 mL/min/1.73m2) and smaller than CKD-EPI_{2021}CrCys (bias IQR 14.4 mL/min/1.73m², p=0.09; median bias 2.3 mL/min/1.73m²), (Fig. 3). A broad range of medications, e.g., immune modulators, and comorbidities, e.g., hypertension, thyroid dysfunction and coronary artery disease, did not interfere with GFR_{NMR} performance.

CONCLUSION

NMR-based eGFR was less biased, more precise and more accurate compared to creatinine and cystatin C CKD-EPI eGFR equations in a post-kidney transplant setting. These findings suggest GFR_{NMR} may more closely resemble mGFR in post-transplant patients and warrants further study on its potential use to improve clinical management in this patient group.

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