Race-Independent eGFR Equations in Assessing Renal Function in Patients with Liver Disease

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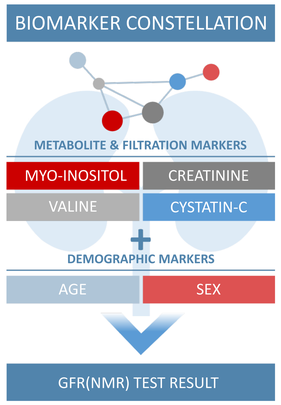
BACKGROUND

Figure 1.



Renal impairment is commonly associated with liver disease, and the degree of renal dysfunction impacts decisions regarding drug dosing, therapeutic interventions, and suitability for liver transplantation. Altered hemodynamics in liver disease often result in overestimation of glomerular filtration rate (GFR) by creatinine-based GFR (eGFR) estimating equations. Recently, we have analytically and clinically validated a novel GFR estimation equation based on serum myo-inositol, valine, and creatinine quantified by nuclear magnetic resonance (NMR) spectroscopy in combination with cystatin C, age and sex *(Fig. 1)*. GFR(NMR) had a lower bias to tracer measured GFR (mGFR) than existing eGFR equations, with a median bias (95% confidence interval [CI]) of 0.0 (1.0; 1.0) mL/min/1.73 m². We demonstrated analytical performance of the novel GFR(NMR) test according to Clinical and Laboratory Standards Institute (CLSI) guidelines including compatible CVs, sample stability consistent with clinical settings, and no clinically relevant interferences from substances. Pre-separation for individual biomarker measurements is not required. We hypothesized that GFR(NMR) improves CKD classification in chronic liver disease (CLD).

METHODS

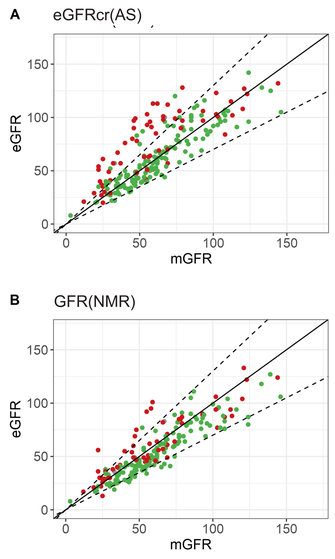
We compared GFR estimation equations in a multicenter retrospective study of patients with liver disease and mGFR. Stored serum was analyzed and used to estimate GFR based on GFR(NMR) (Numares, Regensburg, Germany), CKD-EPI 2021 eGFRcr-cys, and CKD-EPI 2021 eGFRcr. The performance of eGFR equations was evaluated according to liver dysfunction severity based on the Child-Pugh (CP) score and the presence or absence of ascites. Preserved liver function was defined by a CP class A without ascites. Reduced liver function was defined by a CP class A with ascites, or a CP class B or C. A total of 205 samples were included in this analysis, collected from CLD patients in Rochester, MN, U.S. (n=155) and Lyon, France (n=50). The study was conducted according to Declarations of Helsinki and Istanbul, and was approved by the Institutional Review Boards (Mayo Clinic IRB# 19-003513, and Hospital Edouard Herriot IRB# DC-2012-1615). All individuals gave informed consent before joining the study.

RESULTS

GFR(NMR) outperformed all other equations with a low overall median bias (-1 vs. -6 to 4 mL/min/1.73 m² for the other equations; $p < 0.05$, *Fig. 2*) and the lowest difference in bias between reduced and preserved liver function (-3 vs. -16 to -8 mL/min/1.73 m² for other equations, *Fig. 3*). Concordant classification by CKD stage was highest for GFR(NMR) (59% vs. 48% to 53%) and less biased in estimating CKD compared to the other equations.

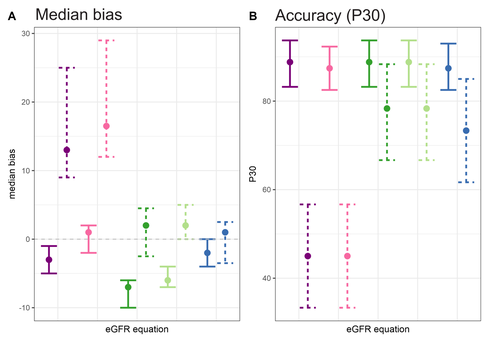
RESULTS (CONT.)

Figure 2. Scatterplot of eGFRcr(AS) vs. mGFR according to liver function.



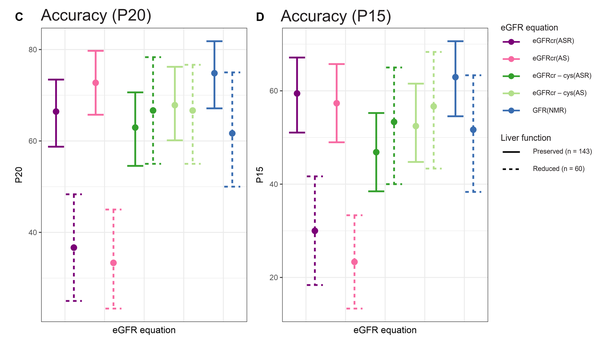
Estimated GFR calculated for eGFRcr(AS) *(Fig. 2A)* and GFR(NMR) *(Fig. 2B)* is shown relative to the respective mGFR. The solid line indicates identity. (AS) = age and sex. Dashed black lines indicate P30 boundaries. Red dots indicate patients with reduced liver function (Child-Pugh Class A with ascites, or Child- Pugh Class B, or Child-Pugh Class C; n=60). Green dots indicate patients with preserved liver function (Child-Pugh Class A without ascites; n=143).

Figure 3. Performance for each eGFR equation stratified by liver function.



RESULTS (CONT.)

Figure 3. (cont.)



Median bias of eGFR to mGFR (A) and accuracy of eGFR measured as the percentage of samples with eGFR within 30% (P30) (B), 20% (P20) (C), and 15% (P15) (D) of mGFR. Purple and pink encode creatinine-only equations, dark and bright green encode creatinine and cystatin C containing equations, and blue encodes the GFR(NMR) equation.

CONCLUSION

Prior study data has shown superior clinical performance of the GFR(NMR) test in accurately detecting kidney function compared to existing eGFR equations. In this study we demonstrated that creatinine-based equations were inaccurate in estimating GFR in patients with CLD. Despite the incorporation of cystatin C, errors are still seen especially with regards to accurate staging of CKD and in patients with more advanced liver disease. Additional metabolites measured by NMR spectroscopy improve on shortfalls of creatinine- and cystatin C-based equations, particularly with regards to accuracy and bias.

*Available as a CE-labeled in vitro diagnostic product in the European Union and for Research Use Only in the U.S. Numares products have not yet been approved or cleared by the U.S. Food and Drug Administration. Poster presented at Kidney Week 2022, Orlando, Florida. Poster TH-PO731.

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