A Multi-Parametric NMR based GFR Estimating Equation for Use in Patients with Liver Disease

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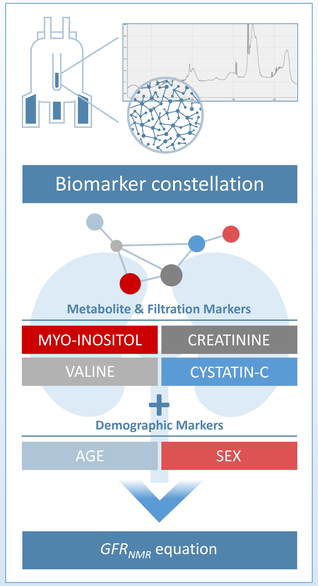
BACKGROUND



Accurate assessment of glomerular filtration rate (GFR) is critical to decision making in individuals with liver disease. Renal impairment is common in association with liver disease and the degree of renal dysfunction impacts decisions on drug dosing, therapeutic interventions, and suitability for liver transplantation. Altered hemodynamics in liver disease often results in overestimation of GFR when using creatinine based GFR estimating equations. Recently, we have developed a novel GFR equation (GFR_{NMR}), which utilizes serum myo-inositol, valine and creatinine quantified by nuclear magnetic resonance spectroscopy (NMR) in combination with Cystatin-C, age and sex. This equation outperforms many GFR estimating equations in chronic kidney disease.

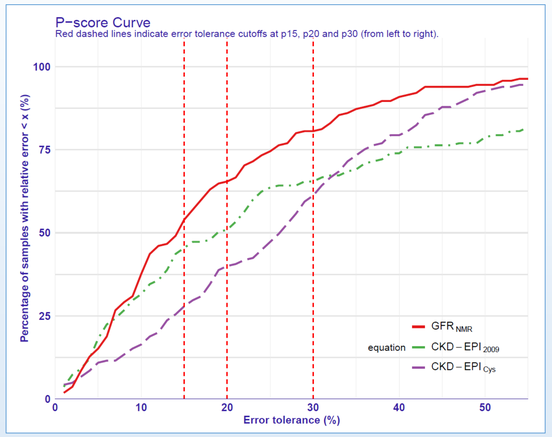
METHODS

We compared various GFR estimation equations including GFR_{NMR} in end-stage liver disease patients scheduled for orthotropic liver transplantation (OLT) in a multicenter retrospective study. In, n=165, liver recipients, renal tracer clearance (mGFR by iothalamate, iohexol or inulin) was measured in preparation of OLT as part of normal clinical care to assess kidney function. We measured Cystatin-C and NMR kidney biomarkers, myo-inositol, valine and creatinine in a single simultaneous measurement. Analytes were used to estimate GFR based on CKD-EPI_{2009}, CKD-EPI_{Cys}, or GFR_{NMR}.

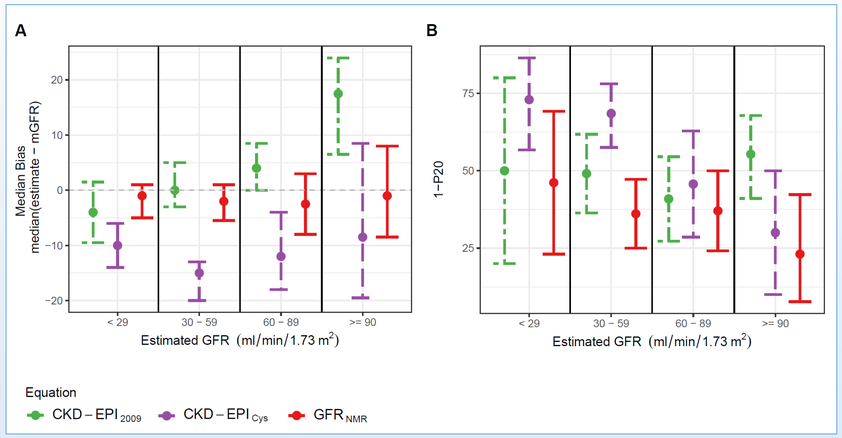
N	165
Age (yrs, range)	18 - 82
Age (yrs, mean ± SD)	58 ± 12
Sex (% male)	65.5
BMI range	16 - 52
BMI mean ± SD	29 ± 7
BMI: < 20	9 (5.5%)
BMI: 20-25	90 (54.5%)
BMI: > 30	66 (40%)
mGFR range	3 - 146
mGFR mean ± SD	65 ± 29
Iothalamate	113 (68.5%)
Iohexol	5 (3%)
Inulin	47 (28.5%)
CKD Stage 1	34 (20.6%)
CKD Stage 2	52 (31.5%)
CKD Stage 3	60 (36.4%)
CKD Stage 4	18 (10.9%)
CKD Stage 5	1 (0.6%)

Characteristics of 165 patients with end-stage liver disease

RESULTS



GFR_{NMR} was superior to CKD-EPI_{2009} and CKD-EPI_{Cys} as shown by the percentage of samples with relative error < 15, 20, or 30% (P15, P20, P30).



GFR_{NMR} showed lower median bias (A) and higher accuracy (B, shown by 1-P20) than CKD-EPI_{2009} and CKD-EPI_{Cys} over the entire GFR range, especially in the clinically relevant range below 60 ml/min/1.73m².

Equation	range	mean±SD	P15 [95% CI]	P20 [95% CI]	P30 [95% CI]	MAE [95% CI]	median Bias [95% CI]
CKD-EPI_{2009}	8 - 142	72 ± 30	44.24 [36.36 - 52.12] ns	50.91 [43.03 - 58.79]*	65.45 [58.2 - 72.73]**	15.28 [12.94 - 17.35]*	3 [-1 - 6]***
CKD-EPI_{Cys}	9 - 120	52 ± 27	27.88 [21.21 - 34.55] ***	40 [33.33 - 47.27]***	61.21 [53.95 - 68.48]**	16.78 [14.83 - 18.58]***	-13 [-16 - -10]***
GFR_{NMR}	9 - 130	62 ± 26	**53.33 [46.67 - 61.21]**	**64.85 [58.18 - 72.12]**	**80.61 [75.15 - 86.67]**	**11.23 [9.57 - 12.71]**	**-2 [-5 - 1]**

Key Performance Indicators of GFR_{NMR} in comparison to CKD-EPI_{2009} and CKD-EPI_{Cys} (MAE: Mean absolute error; CI: Confidence interval)
Significance level adj. p-value, comparison with GFR_{NMR}: ns = not significant; * < 0.01; **< 0.001; ***< 0.0001; significance of differences was calculated via McNemar test for P15, P20 and P30 or Wilcoxon-signed rank test for MAE and median Bias;

CONCLUSIONS

Kidney function assessment is critical in patients wit Liver Diseases. GFR_{NMR} provides a more accurate assessment of GFR estimation over creatinine and Cystatin-C based equations in individuals with liver disease.

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