EMPAKT CHF STUDY – LATE BREAKING POSTER –ASN 2019

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Lack of Concordance Between Changes in the Serum Creatinine and Measured GFR in Patients with Acute Decompensated Heart Failure

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Background

Serum creatinine is frequently used clinically to assess kidney function and to diagnose acute kidney injury (AKI) in patients with acute decompensated chronic heart failure (ADCHF). Unfortunately, creatinine and estimated GFR (eGFR) may not accurately reflect renal function in patients with chronic heart failure and may further be affected by shifts in volume distributions in the context of ADCHF [1] In this study we measured plasma volume (PV) and GFR (mGFR) in patients undergoing decongestive treatment with diuretics for ADCHF and correlated them with eGFR dynamics.

Methods

This multicentric prospective cohort study in 50 hospitalized subjects with ADCHF was conducted at Charité Universitätsmedizin Berlin and Kerckhoff Klinik Bad Nauheim. Subjects aged ≥ 18 years, hospitalized with at least one sign (rales, peripheral edema, ascites, or pulmonary vascular congestion on chest radiography) and one symptom (dyspnea, orthopnea, or edema) of acute decompensated heart failure were enrolled. PV and GFR were measured using a two-component intravenous visible fluorescent injectate (VFI) at two time points 48h apart during the course of treatment. Serum concentrations of a high molecular weight dextran component of VFI were measured 15, 60 and 180min after a single injection to quantify PV using the indicator-dilution principle. At the same time, concentrations of a low molecular weight dextran were measured to determine mGFR based on PV-normalized plasma pharmacokinetics. eGFR was determined using Chronic Kidney Disease Epidemiology Collaboration (CDK-EPI) and Simplified Modification of Diet in Renal Disease Formula (sMDRD)

Pearson correlation coefficients of mGFR and eGFR (CKD-EPI) were calculated. *r2* statistics were used to measure precision and to give an indication of the overall fit of the model. Accuracy was assessed by comparing eGFR with mGFR using the following equation:

(eGFR – mGFR) * 100 / mGFR [2]

and counting the number of subjects with eGFR values within 15% or 30% of the mGFR. Bias was assessed by calculating the mean and standard deviation of the difference between mGFR and eGFR.values.

Results

Baseline Characteristics	All Patients (n=50)
Age	72,5 (13,7)
Male	40 (80)
Caucasian	48 (96)
NYHA I-II	7 (14)
NYHA III-IV	43 (86)
LVEF	47,87 (±15,5)
HFpEF	29 (58)
$eGFR_{BL}$, ml/min	49,8 (21,4)
CKD-Stage, median (IQR)	3 (2-4)
Medication	
β-Blocker	38 (76)
RAS-Inhibitors	31 (62)
AT1/Neprilysin-Inhibitor	7 (14)
Spironolacton	20 (40)
Diuretics	40 (80)
Physical Examination	
Systolic BP, mmHg	126(±24)
Diastolic BP, mmHg	72(±14)
Heart rate, bpm	74(±16)
Weight, kg	86(±22)
BMI kg/m²	30(±6)

Table 1: Baseline characteristics, data are presented as number (%) or mean (Standard Deviation (SD)), HFpEF = Heart Failure with preserved Ejection Fraction, $eGFR_{BL}$= eGFR at Baseline, CKD=chronic kidney disease, RAS= renin-angiotensin system, AT1= Angiotensin-1-receptor blocker, BP = Blood pressure

Baseline characteristics are shown in Table 1. 38 patients had complete serial data regarding GFR dynamics during 48h of treatment While eGFR and mGFR correlated significantly at the time of study inclusion (r=0.829, p<0.01) and after 48h of ADHF treatment (r=0.84, p<0.01) changes of eGFR and mGFR during 48h of treatment did not correlate significantly (r=0,3; p=0.08) (Fig. a-c). 11 patients showed an increase of mGFR, 27 patients showed a decrease of mGFR. In contrast, 17 patients had an increase of eGFR, 5 did not show a change and 16 patients showed a decrease of eGFR.

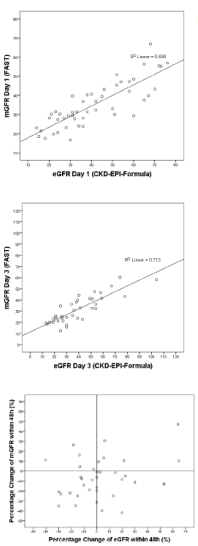

Figure a) Correlation of eGFR and mGFR on Day 1, r=0.83, p<0.01, n=50, Figure b) Correlation of eGFR and mGFR on Day 3, r=0,84, p=0,01, n=38, Figure c) Correlation of Percentage Change of eGFR and mGFR within 48h, r=0,3, p=0,08, n=38, R^2= coefficient of determination

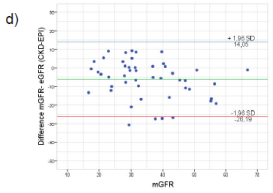

Figure d) Bland-Altman Plot of GFR Day 1 (n=50)

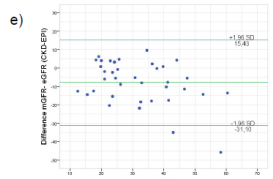

Figure e) Bland-Altman Plot of GFR Day 3 (n=38)

		Precision	Accuracy		Bias
	Mean ± SD	R^2	15%	30%	Mean ± SD
$mGFR_{FAST}$	35 ± 11,7				
$eGFR_{CKD-EPI}$	41,2 ± 17,7	0,69	37,5%	69%	-6,1± 10,3
$eGFR_{sMDRD}$	44,1 ± 17,8	0,68	25%	65%	-9 ±10,6

Table 2 Precision, Accuracy and Bias of estimators of GFR Day 1 (n=50)

		Precision	Accuracy		Bias
	Mean ±SD	R^2	15%	30%	Mean ±SD
$mGFR_{FAST}$	31,9±12,9				
$eGFR_{CKD-EPI}$	39,4±20,4	0,71	27%	65%	-7,8 ±11,6
$eGFR_{sMDRD}$	42,8±20,6	0,77	27%	53%	-11,4 ±11,1

Table 3 Precision, Accuracy and Bias of estimators of GFR Day 3 (n=38)

7 patients (18%) showed a decrease of mGFR by ≥ 25% during 48h of treatment, but only one of these patients showed a corresponding decrease of creatinine-based eGFR (CKD-EPI) by ≥ 25%. Conversely,4 patients showed a decrease of eGFR (CKD-EPI) ≥ 25%, but only one of these patients had a corresponding decrease of measured GFR by ≥25%. Conversely, 4 patients showed a decrease of eGFR ≥ 25%, but only one of these patients had a corresponding decrease of measured GFR by ≥ 25%.
Bland-Altman Plots (Figs. d, e) and bias analyses (Tables 2, 3) showed that eGFR frequently overestimated mGFR. Both eGFR (CKD-EPI) and eGFR (sMDRD) showed a low precision and accuracy (Tables 2 and 3).

Conclusions

In patients hospitalized for ADCHF undergoing recompensation, measured GFR and changes of mGFR displayed a remarkable disconnect from estimated GFR predictions. Serum creatinine-based KDIGO AKI criteria frequently provided GFR-independent false-positive signals, indicating a need for improved diagnostics to identify worsening GFR and refined detection of AKI using measures of kidney filtration and markers of kidney damage in these patients.

References:
[1] House, A.A., et al., Heart failure in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int, 2019. 95(6): p. 1304-1317.
[2] Bostom AG, Kronenberg F, Ritz E. Predictive performance of renal function equations for patients with chronic kidney disease and normal serum creatinine levels. J Am Soc Nephrol. 2002;13 2140–2144

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