Both Cystatin C and Creatinine overestimate renal function in patients with primary neuromuscular disease

[1]Annika Aldenbratt, [2]Christopher Lindberg, [1]Maria K Svensson.
[1]Department of Nephrology, Sahlgrenska University Hospital, Gothenburg, Sweden,
[2]Neuromuscular Center/Department of Neurology, Sahlgrenska University Hospital, Gothenburg, Sweden

BACKGROUND

Estimated renal function based on serum creatinine can be falsely overestimated in patients with primary neuromuscular disorders and reduced renal function may remain undetected.
Cystatin C, another marker of renal function, may be a better marker of renal function in patients with primary neuromuscular disorders.

AIM

To evaluate the precision, accuracy and bias for three different creatinine-, one cystatin C- and one combination-based estimation of renal function in patients with primary neuromuscular disorders.

PATIENT AND METHOD

145 patients (68 M, 77 W), mean (sd) age 46 (14), BMI 26 (6) kg/m^2 with a primary neuromuscular disease* were included. GFR was measured by iohexol clearance (mGFR) and blood samples for analysis of serum creatinine and cystatin C were drawn simultaneously as clearance was done. (Table 1.) Bias was assessed as the mean difference between estimated GFR (eGFR) and mGFR with positive values indicating overestimation of mGFR. Accuracy was defined as the proportion of eGFRs within ±10% (P10) and ±30% (P30) of mGFR.

Table 1. Clinical and biochemical characteristics of study participants (n=145).

	Mean ± SD	Range
Gender		
Male 68 (47%) Female 77 (53%)		
Age (year)	46 ± 14	(18-79)
Weight (kg)	76 ± 18	(34-129)
Length (cm)	171 ± 10	(144-210)
Body mass index (BMI) (kg/m^2)	26 ± 6	(13-47)
Systolic bloodpressure (mmHg)	123 ± 19	(85-190)
Smooth muscle mass index (SMI)	6.2 ± 2.1	(5.6-10.5)
S-cystatin C (mg/L)	0.96 ± 0.17	(0.60-1.69)
S-creatinine (µmol/L)	58 ± 24	(7-144)
mGFR (ml/min/1.73m^2)	81 ± 19	(38-134)
MDRD (ml/min/1.73m^2)	169 ± 177	(36-1203)
CKDEpi (ml/min/1.73m^2)	116 ± 36	(41-291)
C-G (ml/min/1.73m2)	181 ± 135	(48-803)
eGFRCysC (ml/min/1.73m^2)	104 ± 25	(12-203)
Diagnosis of primary neuromuscular disease		
Becker muscular dystrophy (BMD)	3	(2.1%)
Myotonic dystrophy type 1 (DM1)	94	(64.8%)
Duchenne muscular dystrophy (DMD)	3	(2.1%)
Fascio scapulo humeral muscular dystrophy (FSHD)	19	(13.1%)
Limb girdle muscular dystrophy (LGMD)	15	(10.3%)
Spinal muscular atrophy (SMA)	11	(7.6%)

Data are mean ± Std (range); mGFR; measured glomerular filtration rate, MDRD; modification of diet in renal disease study group , CKDEpi; chronic kidney disease epidemiology collaboration, see methods section.
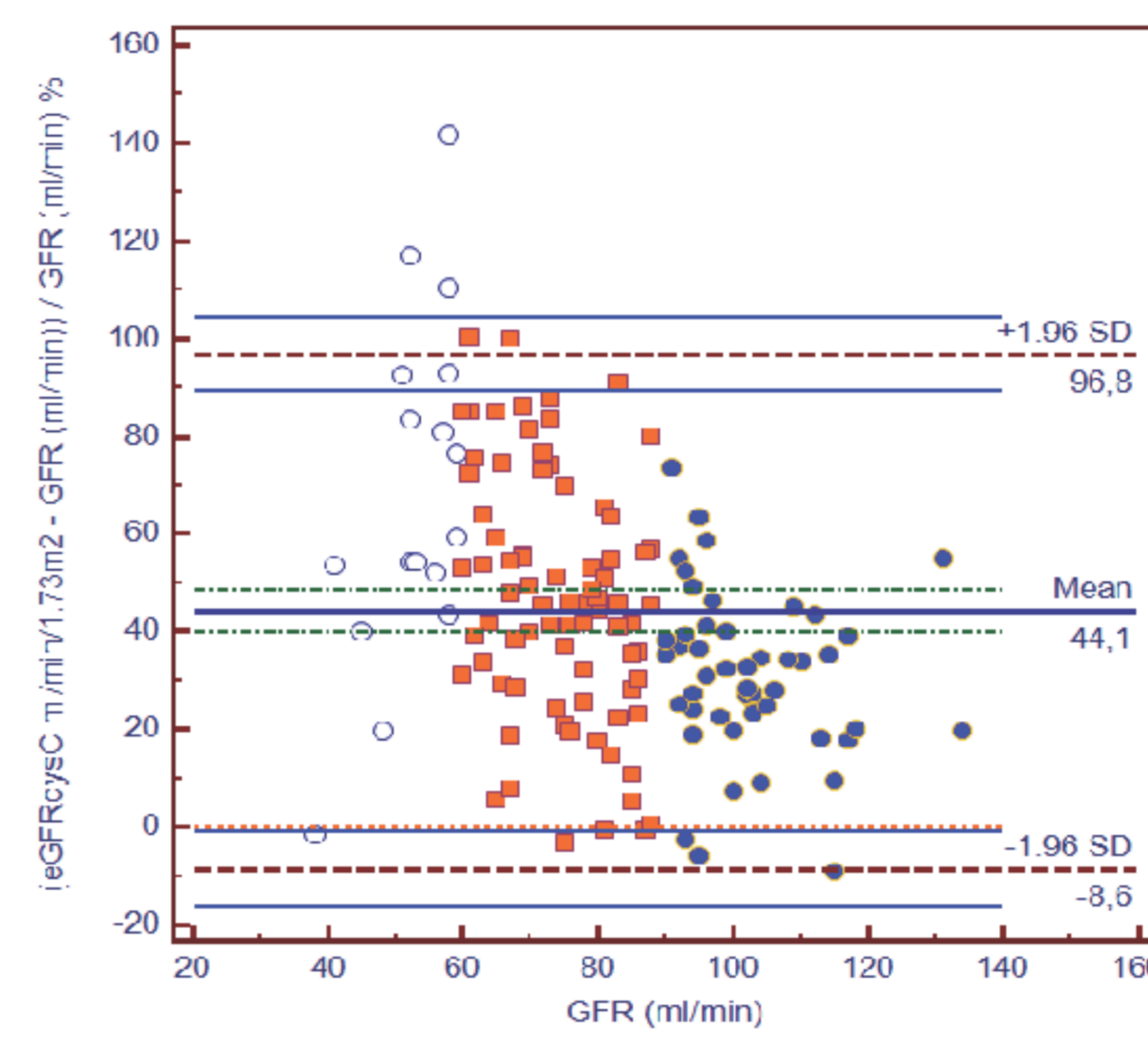

Diagram 1.
Bland-Altman diagram comparing the difference between estimated GFR for Cystatin C (eGFRCys C) and measured GFR (mGFR) by iohexol clearance.
GFR levels as indicated;
O = 38-59 ml/min/1.73m^2
■ = 60-89 ml/min/1.73m^2
● = 90≥ ml/min/1.73m^2

Table 2. Different levels of measured glomerular filtration rate (mGFR) (ml/min/1.73m^2).

	Overall (n=145)	30-59 (n=18)	60-89 (n=79)	90≥ (n=48)
Accuracy (P10)[b] (%)				
MDRD	6.2 (2.8, 11.1)*	0.0 (0.0, 0.0)	6.3 (1.5, 11.5)*	8.3 (1.9, 17.4)
CKDEpi	11.0 (6.2, 16.5)	0.0 (0.0, 0.0)	7.6 (2.4, 13.7)*	4.2 (0.0, 11.1)
C-G	6.9 (3.4, 11.0)*	0.0 (0.0, 0.0)	10.1 (4.0, 17.7)	20.8 (10.3, 32.6)
eGFRCysC	20.8 (14.6, 27.8)*	11.8 (0.0, 30.0)	8.9 (2.8, 15.8)	43.8 (29.5, 58.1)*
eGFRCysC + CKDEpi	16.0 (10.4, 22.0)	5.6 (0.0, 17.6)	19.0 (11.1, 27.3)	14.6 (4.7, 24.4)
Accuracy (P30)[b] (%)				
MDRD	38.6 (31.0, 46.2)	22.2 (4.5, 43.8)	41.8 (30.4, 53.4)	39.6 (26.0, 55.4)
CKDEpi	37.9 (27.9, 45.5)	11.1 (0.0, 27.3)	31.6 (21.3, 43.0)*	58.3 (45.0, 71.2)*
C-G	20.1 (13.9, 27.1)*	16.7 (0.0, 36.3)	20.3 (11.7, 28.9)*	20.8 (9.8, 32.8)*
eGFRCysC	47.2 (38.9, 54.9)	17.6 (0.0, 38.5)	36.7 (26.7, 46.8)	75.0 (62.5, 86.4)*
eGFRCysC + CKDEpi	38.6 (31.0, 46.9)	22.2 (5.3, 44.4)	41.8 (31.6, 53.7)	39.6 (26.5, 54.1)

RESULT

Measured GFR (mGFR) was mean (sd) 81 (19), range 38-134 ml/min/1.73m^2. All equations (eGFRCG, eGFRMDRD, eGFRCKDEpi, eGFRCysC and eGFRCysC+CKDEpi) overestimated GFR (22.8 to 60.0 ml/min/1.73m^2). (Diagram 1.)

The overall accuracy for the different equations varied widely (P10 6.2-20.8% and P30 20.1-47.2%) (Table 2.). When comparing the accuracy at different levels of GFR none of the creatinine-based equations had P10 in the patient group with the lowest renal function and P10 for the combinated equation eGFRCysC+CKDEpi was only 5.6%.

eGFRCysC alone had the best accuracy in patients with the lowest renal function (P10 11.8%). At P30, MDRD had the best performance in patients with the lowest renal function (22.2%), CKDEpi was best in patients with GFR≥90 ml/min/1.73m2 (58.3%). The P30 for eGFRCysC was best in patients with normal renal function (75%), the P30 in the patient group with the lowest renal function was not as good, only 17.6%, for eGFRCysC.

CONCLUSION

A cystatin C-based estimation of glomerular filtration rate alone gives the most accurate estimation of renal function in patients with primary neuromuscular disease and low muscle mass. But all equations systematically overestimated renal function and the largest overstimation were found in patients with reduced renal function.

REGION VÄSTRA GÖTALAND
SAHLGRENSKA UNIVERSITY HOSPITAL

UNIVERSITY OF GOTHENBURG

For additional information, please contact: Dr Annika Aldenbratt. E-mail: annika.aldenbratt@vgregion.se.

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J1) Chronic Kidney Disease. Lab methods, GFR measurement, urine proteomics.

Annika Aldenbratt

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