

Quebec Society of Nephrology

**Derivation of a new prediction equation for estimating
glomerular filtration rate in children**

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What is GFR?

- Gold standard method of expressing kidney function.
- KDOQI guidelines use GFR to classify kidney disease stage.

“Gold standard” methods of measuring GFR

- Iothalamate clearance, inulin clearance.
- Nuclear medicine isotope clearance (DTPA, CrEDTA)

GFR prediction equations are important

- KDOQI guidelines recommend to use GFR prediction equations.
- “Gold standard” GFR tests are not practical.
- Serum creatinine is not a good estimate of GFR.

Current child GFR prediction formulas are inadequate

Adult prediction equations

- Cockcroft-Gault, MDRD tested in many populations

Child prediction equations

- *Schwartz:* 1976
Gold standard = 24 hour creatinine clearance
Found not to be accurate or precise
- *Leger:* 2003
Gold standard = Cr EDTA
Not yet validated

Derivation of a new prediction equation
for estimating
glomerular filtration rate in children

Zappitelli M, Joseph L, Gupta I, Boivin J-F, Bell L, Paradis G.

Goals and objectives

- To **derive a prediction equation** for GFR in children, based on SCR and other potential variables, using sound statistical techniques.
- To **evaluate and compare** the performance characteristics of the new equation to those of the Schwartz and Leger formulae.
- To perform a **validation study** of the Leger formula.

Methods

Design, setting, subject selection

- All iothalamate GFR tests from 1999 to 2004 at MCH.
- Inclusion: 2 to 21 years.
- Exclusion: Unreliable GFR result.

Methods

Data collection

- “Gold standard” GFR result.
- **Demographic:** Age and gender
- **Clinical:** Height, weight, presence or absence of spina bifida, diagnosis.
- **Laboratory:** SCR

Methods

Published GFR estimate equations

Schwartz

*k = 0.55 EXCEPT:
boys >13 years : k = 0.7

$$GFR(ml/min/1.73m^2) = k * height/SCR$$

Leger

$$GFR (ml/min) = [(56.7 * weight) + (.142 * height^2)]/SCR$$

Methods

Data management and analysis

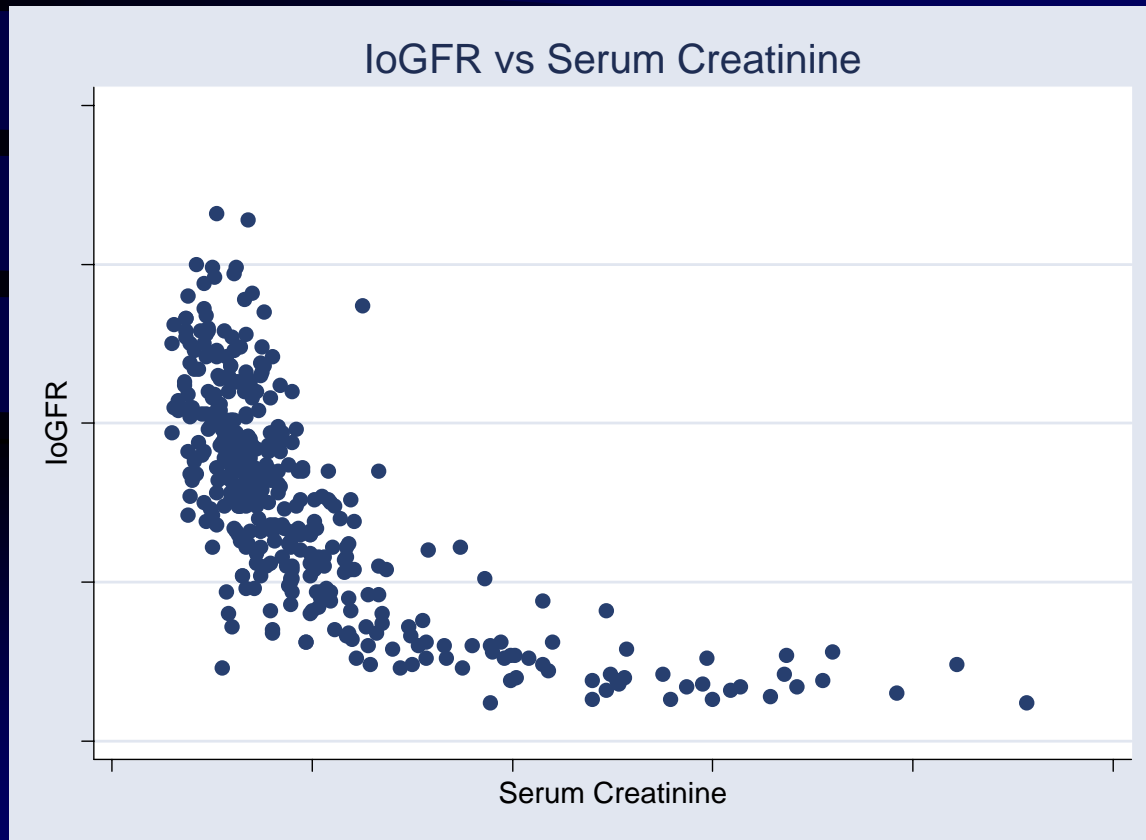
Deriving the equation

independent variable

dependent variable

- The main relationship:

How can **SCR** predict **GFR**?



- Non-linear relationship

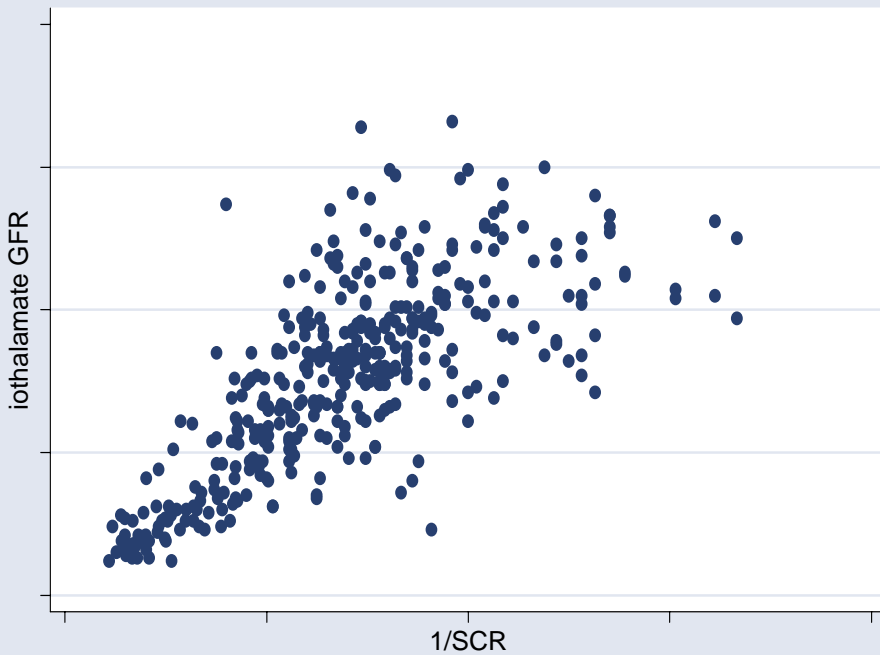
Methods

Data management and analysis

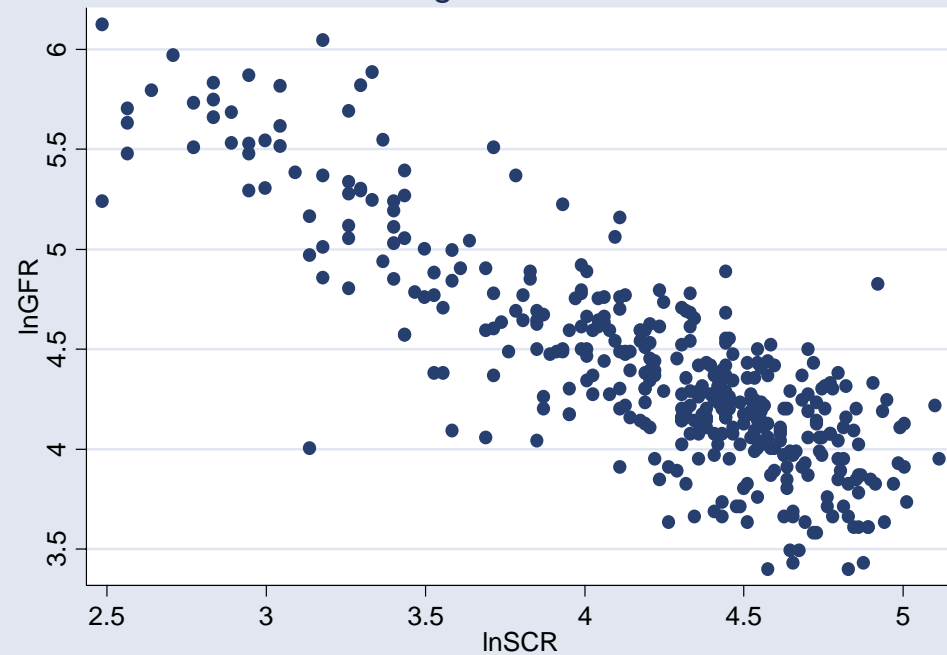
Deriving the equation

Variable transformation

GFR vs 1/SCR



lnGFR vs lnSCR



Methods

Data management and analysis

Deriving the equation

1. Make the equations

“Complex equation”: $\ln\text{GFR} = \text{intercept} + \ln\text{SCR} + \mathbf{x}_1 + \mathbf{x}_2 + \dots$

e.g. height

e.g. spina bifida

“Simple equation”: $\text{GFR} = \text{intercept} + 1/\text{SCR} + \dots$

2. Compare the new equations to existing ones:

Correlation to gold standard GFR

Sensitivity and specificity

Evaluation of bias and precision (Bland Altman)

Results

n = 391 GFR's

n = 207 patients

Patient characteristics.... by diagnosis

Diagnosis	n	age	GFR	% male	Schwartz GFR	Leger GFR
CRF	162	12.4 (4.2)	69.3 (36.7)	60.5%	91.4 (44.5)	86.9 (39.3)
Recent chemo	2	15.4 (4.2)	108.0 (58.0)	100.0%	131.0 (5.5)	117.2 (30.9)
Post renal transplant	115	13.3 (4.4)	78.3 (26.0)	73.0%	94.6 (26.8)	89.6 (25.4)
Post other transplant	69	10.8 (3.9)	89.8 (23.5)	66.7%	119.0 (30.6)	122.5 (35.2)
Cystinosis (pre- transplant)	19	9.5 (2.2)	29.8 (11.7)	68.4%	39.1 (17.5)	43.6 (20.5)
Spina bifida	13	15.6 (3.6)	104.5 (19.9)	30.8%	185.5 (54.5)	171.6 (46.6)
No known renal disease	4	14.6 (6.2)	107.8 (40.3)	25.0%	149.0 (29.7)	154.6 (44.9)
Category unknown	7	7.6 (6.0)	94.0 (36.6)	42.9%	113.4 (31.6)	128.3 (37.3)

Results

“Best equations”

- Based on:

1. BIC

2. a) Sensitivity/specificity to detect GFR 20, 30, 60, 90, 110
b) Level of bias and precision

At different age levels &
At different GFR levels

Eq 49: $\ln GFR = 7.54 - \ln SCR + .008(\text{height})$

** if diagnosed with spina bifida, subtract 4.37 and add 1.07($\ln SCR$)*

Seq 5: $GFR = -61.99 + 4896.96/SCR + .51(\text{height})$

**if diagnosed with spina bifida, add 95.48 and subtract 5288.66/ SCR*

Results

The new equations performed better than the Schwartz and Leger

Item	Eq 49	Seq 5	Schwartz	Leger
Fitted vs true GFR correlation (r)	0.8328	0.8246	0.7659	0.7808
Mean difference (95% CI)	-0.973 (-2.8 to .9) p<0.0001	0.870 (-1.0 to 2.8) p<0.0001	23.123 (20.3 to 25.9)	20.40 (17.8 to 23.0)
CRMSE	18.67	18.9	36.24	33.02
GFR<30				
sensitivity	84.09%	54.55%	52.27%	52.27%
specificity	99.14%	99.71%	100%	100%
% correct	97.44%	94.63%	94.63%	94.63%
GFR<90				
sensitivity	87.35%	90.12%	60.08%	61.66%
specificity	68.12%	68.12%	89.13%	92.75%
% correct	80.56%	82.35%	70.33%	72.64%

Results

The new equations performed better than the Schwartz and Leger...

- Similar findings at different age levels.
 - <6 years
 - 6 to 13 years
 - 13 to 15 years
 - >15 years
- Similar findings at different levels of GFR.
 - <30 ml/min/1.73m²
 - 30 to 60
 - 60 to 90
 - 90 to 110
 - >110

Results

Summary

- 2 new equations for estimating GFR derived from a sample of children with a wide range of renal function:

$$\text{Eq 49: } \ln\text{GFR} = 7.54 - \ln\text{SCR} + .008(\text{height})$$

** if diagnosed with spina bifida, subtract 4.37 and add 1.37(lnSCR)*

$$\text{Se5: } \text{GFR} = -61.99 + 4896.96/\text{SCR} + .51(\text{height})$$

**if diagnosed with spina bifida, add 95.48 and subtract 5288.66/SCR*

- They both:
 - Correlate better than Schwartz and Leger GFR's with true GFR
 - Provide less biased and more precise GFR estimates
- In our group, the Leger GFR equation did not provide more accurate estimates of GFR.

Clinical implications

- A reliable GFR prediction equation for children is needed.
- This equation could be used for GFR prediction in our centre.
- The equation may help us be better at identifying patients with abnormal GFR.

Weaknesses of this study

- From only one centre - ?lack of generalizability to other centres.
- Includes mix of many diagnoses:
Perhaps better to make a different formula for each patient category
- Numbers: higher is always better -- get more precise estimates.
- Not surprising that GFR estimate from my formula works better--
they WERE made by using OUR “true” GFR as a gold standard!

Future directions

- Examine this formula in the different diagnostic groups.
- Attempt to validate in other centres: ? HSJ????

Derivation of a GFR prediction equation based on CysC

n = 109 patients

Same methods