The More Sensitive Alternative to Estimate GFR

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The More Sensitive Alternative to Estimate GFR

Increase Sensitivity and Reliability in Renal Function Analysis

According to the KDIGO* guidelines published in June 2005, glomerular filtration rate (GFR) is used for definition and classification of chronic kidney disease (CKD).

Definition of chronic kidney disease [1]:

- GFR< 60mL/min/1.73 m^2 for ≥ 3 months, or
- Kidney damage for ≥ 3 months (structural or functional abnormalities; e.g. increased albumin excretion)

A reliable and sensitive method for GFR assessment is crucial to diagnose CKD at early stages; strategies to improve outcomes are more successful with earlier treatment. Here cystatin C offers clear advantages over serum creatinine (and creatinine-based GFR formulas) for a sensitive and reliable diagnosis of decreased GFR.

Classification of chronic kidney disease is based on GFR:

Stage	GFR (mL/min/1.73m²)	Cystatin C (mg/L)	Description
1	≥ 90	≤ 0.85	normal or elevated GFR
2	60 - 89	0.86 - 1.25	mild GFR reduction
3	30 - 59	1.26 - 2.34	moderate GFR reduction
4	15 - 29	2.35 - 4.16	severe GFR reduction
5	< 15	> 4.16	renal failure

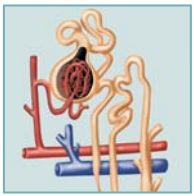
* Kidney Disease: Improved Global Outcome

The More Sensitive Diagnostic Alternative to Estimate the Glomerular Filtration Rate (GFR)

- **Cystatin C: No tubular secretion; sensitive in the creatinine-blind range**[2]
  - Higher sensitivity in early disease
- Creatinine: In early disease, tubular secretion compensates for the decline of glomerular filtration
  - Creatinine blind range; creatinine levels increase only if more than 50% of renal function is lost
  - MDRD* or Cockcroft-Gault formula cannot compensate for this limitation

- **Cystatin C: Independent of age, sex and muscle mass**[2]
  - Constant relationship between Cystatin C and GFR at 1 year of age and older
  - Single reference range: 0.53 – 0.95 mg/L in children and adults
  - No correction parameters required for Cystatin C based formulars for GFR estimation
  - Sensitive detection of declining GFR with aging possible
  - Reliable in patients with spina bifida, paralysis, amputations, etc.
- Creatinine: depends on age, sex, muscle mass
  - Different relationship between creatinine and GFR, between men and women, in children, adults and elderly, and patients with low and high muscle mass
  - Different reference ranges for interpretation
  - Correction for age, sex, race, weight (…) for GFR estimation formulas
  - Due to declining muscle mass in old age, lower sensitivity for loss of renal function with aging
  - Not suited for patients with grossly abnormal muscle mass

* Modification of Diet in Renal Disease



- **Cystatin C: High correlation to GFR reference methods[2], high correlation to GFR decline**
  → High reliability and accuracy
- Creatinine: Correlation to GFR reference methods less accurate, especially in normal or only slightly abnormal GFR
  - Limited reliability, lower sensitivity

- **Cystatin C: Not influenced by liver disease or creatine intake; may be influenced by high dose steroid therapy or thyroid dysfunction**
- Creatinine: Strongly influenced by liver disease; dependent on creatine (= protein) intake

- **Cystatin C: No analytical interferences known**
- Creatinine: Many analytically interfering factors (e.g. bilirubin, ascorbic acid, various drugs) for common analytical methodologies

Patients who may benefit most from GFR assessment using Cycstatin C:

- Children and infants
- Patients at high risk for CKD where monitoring is required, e.g. with diabetes, hypertension, etc.
- Patients with suspicion of mild to moderate reduction of GFR
- Patients at risk for acute renal failure
- Patients with liver disease
- Elderly patients

GFR Estimation from Cystatin C:

A formula for converting Cystatin C values to body surface adjusted eGFR has been described by Hoek et al.[3] The utility of this formula was examined in a population of 123 patients ranging in age from 11 to 77 years, with GFRs (by iothalamathe clearance) ranging from 12 to 157 mL/min/1.73m^2.

$$\mathbf{eGFR}_{CysC}\ (mL/min/1.73m^2) = -4.32 + \frac{80.35}{CysC}$$

Applying this formula, the following conversion table is obtained:

CysC (mg/L)	$eGFR_{CysC}$ (mL/min/1.73m^2)	CysC (mg/L)	$eGFR_{CysC}$ (mL/min/1.73m^2)
0.5	156	1.8	40
0.6	130	1.9	38
0.7	110	2.0	36
0.8	96	2.2	32
0.9	85	2.4	29
1.0	76	2.6	27
1.1	69	2.8	24
1.2	63	3.0	22
1.3	57	3.2	21
1.4	53	3.4	19
1.5	49	3.6	18
1.6	46	4.0	16
1.7	43	4.2	15

Literature:

1. Levey AS et al. Kidney Int 2005; 67: 2089-100.
2. Newman DJ. Ann Clin Biochem 2002; 39: 89-104.
3. Hoek F et al. Nephrol Dial Transplant 2003; 18:2024-31

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