

Cystatin C for GFR

The sensitive marker for glomerular filtration rate (GFR)

Estimation of GFR from Serum Cystatin C:

The good correlation allows close estimation of GFR

Cystatin C in serum (mg/l)	GFR estimated* (ml/min)	GFR measured* mean \pm s (ml/min)	n
0.6	145	125 \pm 34	14
0.7	119	111 \pm 26	31
0.8	99	93 \pm 16	21
0.9	85	84 \pm 27	17
1.0	74	79 \pm 15	21
1.1	65	68 \pm 12	15
1.2	58	61 \pm 16	9
1.3	52	55 \pm 13	15
1.4	47	55 \pm 14	12
1.5 – 1.6	41	40 \pm 19	12
1.7 – 1.8	35	42 \pm 10	9
1.9 – 2.0	30	32 \pm 7	7
2.1 – 2.3	26	34 \pm 6	7
2.4 – 2.6	22	28 \pm 11	5
2.7 – 3.0	18	24 \pm 7	5

* Inulin clearance and serum Cystatin C testing in 209 patients with a broad range of GFR, age and different pathologies yielded the following correlation function for calculation of estimated GFR:

$$\text{GFR estim.} = \frac{74.835}{\text{Cys C}^{1/0.75}}$$

Reference Range for Cystatin C: ≤ 0.95 mg/l in Men & Women

- children > 1 year show adult levels
- higher Cystatin C levels in elderly healthy subjects > 60 years reflect increased sensitivity for the age-related GFR decline
- not influenced by muscle mass or any analytical interfering factors

A.O. Grubb *Adr. Clin Chem* 2001; 35 : 63 – 59

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Cystatin C – the Ideal Marker for GFR:

- **Free glomerular filtration, without tubular secretion**

Cystatin C, a 13,250 D, non-glycosylated protein does not bind to any other plasma protein; the only elimination route for Cystatin C is glomerular filtration.

- **Stable production rate, constant circulating levels**

The Cystatin C expression regulating gene is of the housekeeping type, guaranteeing a stable production rate. Cystatin C is synthesized by all nucleated cells.

Cystatin C is not influenced by an acute phase reaction.

- **No re-entrance into the blood circulation**

Cystatin C is reabsorbed by the tubulus cells and thereby rapidly degraded. In the case of tubulus dysfunction, absorption is impaired and Cystatin C is eliminated with the urine. Therefore, urinary Cystatin C levels can be used as a marker of tubulus dysfunction.

A.O. Grubb Adr. Clin Chem 2001; 35 : 63 -99

- **No extra-renal elimination**

Cystatin C is cleared only via glomerular filtration.

Cystatin C – Preferable to creatinine and creatinine clearance:

Correlation of Cystatin C with GFR not influenced by:

- gender
- muscle mass
- age (children > 1 year of age show adult levels)
- protein intake
- metabolic factors influencing creatinine tests; e.g. bilirubin, ketones, elevated glucose or ascorbic acid
- various drugs interfering with creatinine tests; e.g. cyclosporine A, cephalosporins, aspirin

- **no urine collection**

sensitive GFR determination with 1 serum or plasma sample

- **increased sensitivity**

to even slight impairment of glomerular filtration; already increases significantly in the creatinine blind range

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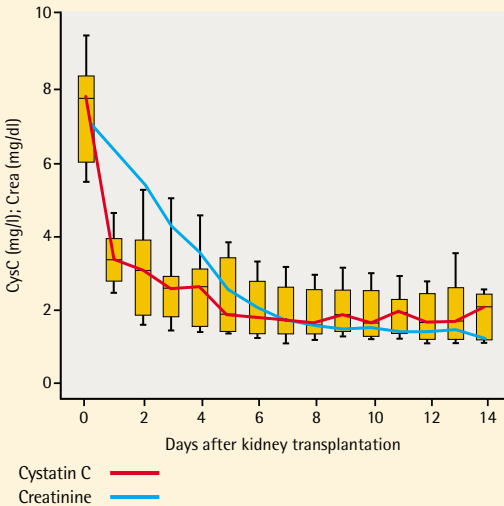
DADE BEHRING

Cystatin C for GFR in Renal Transplantation

The sensitive marker for glomerular filtration rate (GFR)

Monitoring Renal Graft Function with Cystatin C:

Kinetics of Cystatin C decrease in 15 patients exhibiting an uneventful postoperative course:



Expected range in stable renal transplant recipients:

median: 1.75mg/l
10.-90. percentile: 1.17 - 3.03 mg/l

P. E. Wallemaq; Eur. Meeting on Biomarkers of Organ Damage and Dysfunction EMBODY 2000; Cambridge, UK

- The **baseline level** is stable, uneventful transplantation is achieved by Cystatin C 6 days after surgery.
- Cystatin C decreases more steeply than creatinine during the first postoperative days, indicating graft function earlier and more clearly.
- In the absence of complications the **relative change** in Cystatin C during monitoring is less than **20%** (90% conf. range).

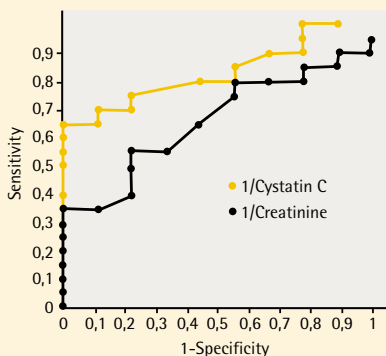
P. E. Wallemaq; Eur. Meeting on Biomarkers of Organ Damage and Dysfunction EMBODY 2000; Cambridge, UK

Cystatin C for GFR in Renal Transplantation

The sensitive marker for glomerular filtration rate

Increased Diagnostic Accuracy after Renal Transplantation:

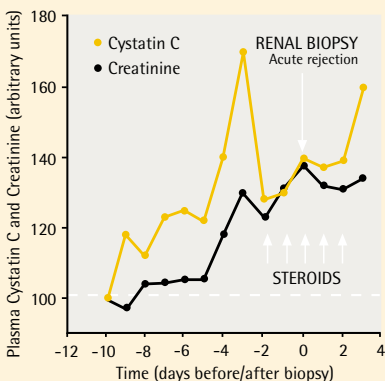
Cystatin C improves discrimination between good and poor graft function



Cutoff = 60 ml/min
GFR measured by
iothalamate
clearance

*L Risch,
Nephrol Dial
Transplant 1999*

Cystatin C rapidly indicates acute rejection and therapeutic response



*T. Le Bricon,
Clin Chem 1999*

"Plasma Cystatin C is an alternative and accurate marker of allograft function in adult transplant patients. Increased sensitivity compared with creatinine for the detection of acute reduction in glomerular filtration rate allows in some cases a more rapid diagnosis of acute rejection or treatment nephrotoxicity."

T. Le Bricon, Clin Chem 1999

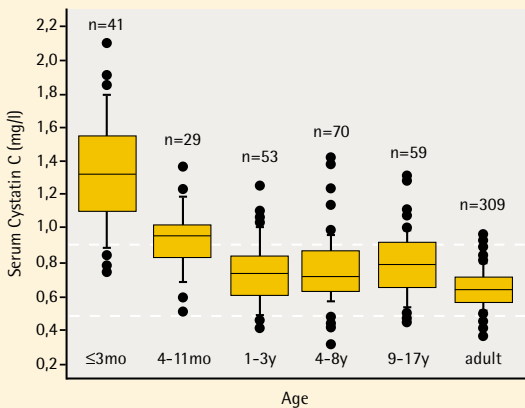
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Cystatin C for GFR in Pediatrics

The sensitive marker for glomerular filtration rate (GFR)

- **No urine collection**
sensitive GFR determination with 1 serum or plasma sample;
no timed collection, no collection errors, assay time 6 min.
 - more reliable than creatinine clearance
 - more rapidly available than creatinine clearance
- **Increased sensitivity**
to even slight impairment of glomerular filtration;
already increases significantly in the creatinine blind range:
 - more sensitive than serum creatinine
- **Age-independent in children > 1 year**
- **Independent of muscle mass/height**
 - less complex interpretation than creatinine or creatinine clearance



D.J. Newman; Ann Clin Biochem 2002; 39 : 89 - 104

Cystatin C for GFR in Pediatrics

The sensitive marker for glomerular filtration rate

Cystatin C – for Reliable and Sensitive GFR Determination in Pediatrics:

- **Sex and muscle mass independent in children > 1 year:**

- adult reference range: 0.53 – 0.95 mg/l Cystatin C
also valid for children > 1 year

H Finney, Arch Dis Child 2000

- **Cystatin C is more closely correlated to reference methods, e.g. inulin or Cr-EDTA clearance**

- increased diagnostic accuracy
- the diagnostic potential of Cystatin C is also superior to that of serum creatinine in children, providing better discrimination of patients with normal and reduced renal function

I Helin, Clin Nephrol 1998

- **Highest Cystatin C levels are observed after birth**

- Cystatin C levels rapidly decline in the first weeks after birth; the high levels in neonates probably reflect the degree of maturation of the glomerula

L Cataldi, Am J Perinatol 1999

- **Cystatin C does not cross the placenta and thus reflects infant renal function**

- no significant correlation between Cystatin C and maternal and neonatal variables, such as weight, BMI, age of mother, sex, diet, gestational age of neonate
- not influenced by maternal serum level, in contrast to creatinine. Preterm infants have higher Cystatin C levels than full-term neonates

L Cataldi, Am J Perinatol 1999

- fetuses with impaired renal function have higher Cystatin C levels than healthy controls

A. Bökenkamp, Am J Obstet Gynecol 2001