Cystatin C: What is its Role in Estimating GFR?

Introduction

How is kidney function determined?

There are several ways in which the kidney’s ability to perform its function is determined. For example, serum creatinine is a commonly used measure of kidney function. The measurement of serum creatinine is often used to determine if someone has kidney disease. However, because serum creatinine is affected by many factors such as muscle mass, diet, and age, it can be difficult to determine if someone truly has kidney disease. For this reason, other measures such as cystatin C are being explored to estimate GFR. Cystatin C, a non-glycosylated 13 kDa protein, is a cysteine protease inhibitor that blocks distal tubule secretion of creatinine (eg, trimethoprim, cimetidine, cefoxitin), the primary urinary excretory route for creatinine. If the patient with advanced CKD takes a substance that blocks distal tubule secretion of creatinine, the serum creatinine level will increase abruptly, but the actual GFR will not change.

The primary limitation of serum creatinine is that it is not a good marker of GFR because it is influenced by factors such as muscle mass and diet. In contrast, cystatin C is a better marker of GFR because it is not influenced by muscle mass or diet. However, the measurement of cystatin C is more expensive than the measurement of serum creatinine. It will take more research to find out which of the many available serum markers is best for estimating GFR.

What patient populations would benefit from using cystatin C in GFR estimating equations?

Cystatin C, serum cystatin C, or cystatin C-based equations are being explored to estimate GFR. Cystatin C more accurately than those that use both creatinine and cystatin C more accurately than those that use only one of these serum markers. Cystatin C-based equations are not precise, so other substances, such as cystatin C, are being explored to estimate GFR. GFR determinations by creatinine-based equations are not precise, so other substances, such as cystatin C, are being explored to estimate GFR. Cystatin C, a non-glycosylated 13 kDa protein, is a cysteine protease inhibitor that blocks distal tubule secretion of creatinine (eg, trimethoprim, cimetidine, cefoxitin), the primary urinary excretory route for creatinine. If the patient with advanced CKD takes a substance that blocks distal tubule secretion of creatinine, the serum creatinine level will increase abruptly, but the actual GFR will not change. The “gold standard” for estimating GFR, over one-third of type 1 diabetes patients have kidney damage, with no false-negative results. The addition of age, sex, and race to cystatin C helps make it a good marker of GFR.


WHAT IS THE ROLE OF CYSTATIN C IN ESTIMATING GFR?

Cystatin C is a cysteine protease inhibitor that blocks distal tubule secretion of creatinine. It is not influenced by muscle mass or diet. However, the measurement of cystatin C is more expensive than the measurement of serum creatinine. It will take more research to find out which of the many available serum markers is best for estimating GFR.

Cystatin C has been evaluated as a marker for chronic kidney disease (CKD) and has been shown to be a better marker than serum creatinine for detecting decreases in GFR. Cystatin C is less influenced by muscle mass and diet than serum creatinine. Cystatin C-based equations are not as precise as those that use both creatinine and cystatin C, and the potential to make cystatin C-based equations more accurate than those that use only one of these serum markers is being explored. However, the measurement of cystatin C is more expensive than the measurement of serum creatinine. It will take more research to find out which of the many available serum markers is best for estimating GFR.

The primary limitation of serum creatinine is that it is not a good marker of GFR because it is influenced by factors such as muscle mass and diet. In contrast, cystatin C is a better marker of GFR because it is not influenced by muscle mass or diet. However, the measurement of cystatin C is more expensive than the measurement of serum creatinine. It will take more research to find out which of the many available serum markers is best for estimating GFR.
Cystatin C: What is its role in estimating GFR?

Introduction

How is kidney function determined?

Chronic kidney disease (CKD) is defined as kidney damage that has lasted for 3 months or more, or kidney damage for 3 months or more with GFR levels below 60 mL/min/1.73 m². CKD may be classified into five stages based on the glomerular filtration rate (GFR), which is defined as the volume of plasma cleared of a given substance per minute. In stage 1 CKD, the GFR is normal, while in stage 2 CKD, the GFR is slightly decreased. In stage 3 CKD, the GFR is moderately decreased. In stage 4 CKD, the GFR is severely decreased, and in stage 5 CKD, the GFR is very low, resulting in kidney failure.

WHAT IS THE ROLE OF GFR IN CKD?

GFR is essential for the diagnosis and management of CKD. A decrease in GFR can indicate the presence of kidney disease, and it can be used to determine the stage of CKD. GFR can also be used to monitor the progression of kidney disease and to assess the effectiveness of treatments.

The addition of age, sex, and race to cystatin C helps make it a superior marker of GFR. Using it in combination or separately could potentially lead to more accurate estimates of GFR. The use of cystatin C in addition to serum creatinine may be advisable, especially at higher GFRs.

However, recent findings suggest that cystatin C-based estimates of GFR at stages 1 and 2 are better correlated with other markers of kidney function, such as albuminuria or proteinuria, than creatinine-based estimates of GFR at stages 1 and 2. In addition, CysC–GFR after transplant has been used to detect allograft rejection and monitor drug nephrotoxicity, with reported diagnostic accuracy of 80% to 90%.

Serum cystatin C has been reported to outperform serum creatinine in detecting decreases in GFR. It has also been shown to have prognostic value for detecting kidney disease and monitoring diabetes and chronic kidney disease. Follow-up cystatin C results have shown that CysC–GFR can provide a clear picture of the patient's disease progression.

An equation that uses both serum creatinine and cystatin C and accounts for race, age, and sex may be even more precise than any one of these factors alone.

The same serum creatinine, very different GFRs?

Serum creatinine levels may vary greatly due to different factors such as muscle mass, diet, age, and race. Additionally, serum creatinine levels can be affected by medications and other substances that interfere with its measurement. Therefore, it is important to use cystatin C in combination with other markers to estimate GFR accurately.

Accurate estimation of glomerular filtration rate (GFR) is essential for the diagnosis and management of CKD. Cystatin C is a low-molecular-weight protein that is filtered at the glomerulus and is not reabsorbed or secreted by the tubules. It is therefore not influenced by muscle mass or diet, and it is excreted in the urine at a constant rate. This makes it a better marker of GFR than serum creatinine.

In conclusion, cystatin C is a promising marker for estimating GFR in patients with CKD. It is a low-molecular-weight protein that is filtered at the glomerulus and is not reabsorbed or secreted by the tubules. It is therefore not influenced by muscle mass or diet, and it is excreted in the urine at a constant rate. This makes it a better marker of GFR than serum creatinine.

Evaluating kidney function also involves measuring the clearance of an exogenous substance such as inulin. The "gold standard" for determining GFR is to measure the clearance of an exogenous substance, such as inulin, over a period of time.

However, the measurement of the clearance of an exogenous substance such as inulin is too time-consuming, and the clearance of an endogenous substance such as creatinine is less influenced by muscle mass or diet. While the renal clearance of creatinine has been shown to be a good marker of GFR, it is important to use cystatin C in combination with other markers to estimate GFR accurately.

The primary limitation of creatinine is that levels are too high in patients with CKD due to muscle wasting or dietary changes. In contrast, cystatin C levels are not influenced by muscle mass or diet, and they are also not affected by diet.

In conclusion, cystatin C is a promising marker for estimating GFR in patients with CKD. It is a low-molecular-weight protein that is filtered at the glomerulus and is not reabsorbed or secreted by the tubules. It is therefore not influenced by muscle mass or diet, and it is excreted in the urine at a constant rate. This makes it a better marker of GFR than serum creatinine.

Why could cystatin C be a good marker of GFR?

Cystatin C has several traits as a marker of GFR:

1. It is a low-molecular-weight protein that is filtered at the glomerulus and is not reabsorbed or secreted by the tubules. It is therefore not influenced by muscle mass or diet.
2. It is measured in serum, which is easy to obtain.
3. It is not affected by the use of nephrotoxic drugs, which can affect creatinine levels.
4. It is not affected by diet, which can affect creatinine levels.
5. It is not affected by muscle mass, which can affect creatinine levels.
6. It is not affected by protein intake, which can affect creatinine levels.
7. It is not affected by obesity, which can affect creatinine levels.
8. It is not affected by age, which can affect creatinine levels.
9. It is not affected by sex, which can affect creatinine levels.
10. It is not affected by race, which can affect creatinine levels.
11. It is not affected by gender, which can affect creatinine levels.
12. It is not affected by pregnancy, which can affect creatinine levels.
13. It is not affected by lactation, which can affect creatinine levels.
14. It is not affected by fasting, which can affect creatinine levels.
15. It is not affected by smoking, which can affect creatinine levels.
16. It is not affected by alcohol consumption, which can affect creatinine levels.
17. It is not affected by exercise, which can affect creatinine levels.
18. It is not affected by dehydration, which can affect creatinine levels.
19. It is not affected by diuretics, which can affect creatinine levels.
20. It is not affected by medications, which can affect creatinine levels.

Most important, it is measured in serum, which is easy to obtain.

Moreover, information is needed, however, to determine how determined it is in certain situations.

In conclusion, cystatin C is a good marker of GFR because it is not influenced by muscle mass or diet, and it is measured in serum, which is easy to obtain.

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Introduction

How is kidney function determined?

The measure most closely linked to the kidney's ability to filter the blood is the glomerular filtration rate (GFR). The GFR is defined as the volume of plasma that is completely cleared of a particular substance by the kidneys in a unit of time.

The clearance of an exogenous substance such as inulin is usually used to determine GFR. Using the new equation could decrease false-positive results, especially at higher GFRs. The primary limitation of the MDRD Study equation, compared to some other equations, is that levels are overestimated 30% when derived from serum creatinine estimates of GFR tend to be less influenced by muscle mass or diet.

Serum creatinine is the most commonly used marker for serum creatinine concentration. The concentration of creatinine in the serum is dependent on several factors, including the measurement of creatinine and other factors, such as creatinine clearance.

Using cystatin C in GFR estimation equations is also present in some current formulas. However, the measurement of cystatin C is not excreted in the urine.

Recent studies suggest that cystatin C may be a better marker of GFR than serum creatinine. Several meta-analyses have concluded that cystatin C may be a better marker of GFR than serum creatinine; still others add age, race, and sex, with or without cystatin C alone, others add cystatin C to creatinine in estimating GFR. The team reported.

An equation that both uses creatinine and cystatin C (age, sex, and race may be better than equations that use only one of these serum markers.5 An equation that uses both serum creatinine and cystatin C with age, sex, and race may be better than equations that use only one of these serum markers.

Cystatin C is a non-glycosylated 13 kDa protein that is produced continuously by all nucleated cells and filtered only by the kidneys. Because it is not secreted by the renal tubules, it maintains a plasma level that is inversely related to the glomerular filtration rate (GFR). The cystatin C concentration is more constant than serum creatinine because it is not affected by muscle mass, metabolism, or diet. In addition, serum cystatin C levels are not affected by muscle wasting, amputation, or azotemia.

Cystatin C has been reported to be a good marker of renal function in patients with chronic kidney disease (CKD), and it is currently being explored to estimate GFR. Cystatin C, a non-glycosylated 13 kDa cystatin C, is produced continuously by all nucleated cells and filtered only by the kidneys.

The cystatin C concentration is more constant than serum creatinine because it is not affected by muscle mass, metabolism, or diet. In addition, serum cystatin C levels are not affected by muscle wasting, amputation, or azotemia.

Cystatin C may provide the best estimation of GFR. In a recent study by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative, cystatin C was more likely to correctly predict that a patient had moderate (CKD 3) or severe (CKD 4 or 5) kidney disease than serum creatinine. However, the measurement of cystatin C is not excreted in the urine.

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative, cystatin C was more likely to correctly predict that a patient had moderate (CKD 3) or severe (CKD 4 or 5) kidney disease than serum creatinine. However, the measurement of cystatin C is not excreted in the urine.

The limitations of cystatin C estimation equations are reviewed by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative, and cystatin C is currently being explored to estimate GFR.
**Cystatin C: What is its Role in Estimating GFR?**

**Introduction**

How is kidney function determined?

Kidney function is commonly assessed using serum creatinine, which is used to estimate glomerular filtration rate (GFR). However, creatinine levels can be influenced by muscle mass, diet, and other factors, leading to potential inaccuracies in GFR estimation.

**Questions**

1. What are the potential limitations of using cystatin C in GFR estimation?
2. Are cystatin C-based equations more precise than creatinine-based equations?
3. Could cystatin C be a good marker of GFR?

**What is cystatin C?**

Cystatin C is a non-glycosylated protein with a molecular weight of 13 kDa, predominantly found in extracellular fluids. It is secreted by most nucleated cells and is filtered at the glomerulus. Cystatin C is present in the bloodstream in low concentrations and is not influenced by muscle mass or diet.

**Why could cystatin C be a good marker of GFR?**

Cystatin C has several advantages over serum creatinine:

1. It is less influenced by muscle mass and diet.
2. It can be measured in a point-of-care setting.
3. It can be used to estimate GFR in patients with low creatinine levels.

**How is cystatin C used in estimating GFR?**

Cystatin C is used in combination with age, sex, and race in estimating GFR. The addition of age, sex, and race to cystatin C helps make it more accurate. However, more research is needed to find out which of the cystatin C-based equations are most reliable and accurate.

**OTHER LIMITATIONS OF CREATINE-BASED GFR**

- GFR changes in kidney function are not immediately apparent.
- Cystatin C decreases to a lower level than creatinine by 15% in the first week after the damage occurs.
- Cystatin C is less useful in the early stages of kidney damage.
- Cystatin C may provide an early warning of kidney damage and be more useful in the early stages of CKD.

**Using Cystatin C: Clinical Considerations with Varying Degrees of Kidney Function**

- Normal: GFR >90 mL/min/1.73 m²
- Moderate Impairment: GFR 60-89 mL/min/1.73 m²
- Severe Impairment: GFR 30-59 mL/min/1.73 m²
- ESRD: GFR <30 mL/min/1.73 m²

**Table 1: Chronic Kidney Disease: Classification by Severity**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>Clinical Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal</td>
<td>&gt;90</td>
<td>No modifications needed</td>
</tr>
<tr>
<td>2</td>
<td>Mild Impairment</td>
<td>60-89</td>
<td>Modify diet and lifestyle</td>
</tr>
<tr>
<td>3</td>
<td>Moderate Impairment</td>
<td>30-59</td>
<td>Begin renal replacement therapy</td>
</tr>
<tr>
<td>4</td>
<td>Severe Impairment</td>
<td>&lt;30</td>
<td>Dialysis therapy</td>
</tr>
<tr>
<td>5</td>
<td>ESRD</td>
<td>&lt;15</td>
<td>Renal transplantation</td>
</tr>
</tbody>
</table>

**GFR, glomerular filtration rate; ESRD, end-stage renal disease**

**Additional Information**

- Cystatin C can provide early warning of kidney damage.
- More research is needed to find out which of the cystatin C-based equations are the most reliable and accurate.
- Cystatin C can be a useful marker of GFR in patients with low creatinine levels.

**Abbreviations:**

- GFR, glomerular filtration rate
- ESRD, end-stage renal disease
- AKI, acute kidney injury
- CKD, chronic kidney disease
- NKF-KDOQI, National Kidney Foundation—Kidney Disease Outcomes Quality Initiative
- GFR-estimating equations, equations used to estimate GFR
- MDRD Study, Modification of Diet in Renal Disease Study
- Cystatin C, a non-glycosylated protein with a molecular weight of 13 kDa
- Serum cystatin C, a marker of GFR
- Point-of-care testing, testing performed at the patient’s bedside

**Source:** National Kidney Foundation.
Cystatin C Equations

1. The original MDRD study equation:  
   \[ \text{eGFR} = 186 \times \left( \frac{\text{SCr}}{1.73} \right)^{-1.154} \]

2. The "renormalized" MDRD study equation:  
   \[ \text{eGFR} = 175 \times \left( \frac{\text{SCr}}{1.73} \right)^{-1.154} \]

3. The CKD-EPI cystatin C equation:  
   \[ \text{eGFR} = 127.7 \times \text{Cystatin C} \]

4. The CKD-EPI cystatin C equation:  
   \[ \text{eGFR} = 76.7 \times \text{Cystatin C} - 0.65 \times \text{age} - 0.20 \]

(equation valid for patients aged 18-90, and for females, multiply by 0.85)

Using Cystatin C: Clinical Considerations with Certain Diseases

1. Thyroid Function, Hyperthyroidism

2. Cardiovascular Disease

3. Kidney Failure, Renal Transplantation

Preliminary Results About Cystatin C in Various Patient Populations

1. Females with Cystatin C concentrations in the upper tertile had a significantly increased risk of developing cardiovascular disease compared to those with lower concentrations.

2. Patients with cystatin C levels above a certain threshold had a higher risk of developing myocardial infarction within a specific time frame.

3. Cystatin C was found to be an independent predictor of cardiovascular events in a cohort of patients with diabetes.

Production of Adverse Events

High cystatin C levels have been associated with an increased risk of adverse events, including cardiovascular events, in patients with chronic kidney disease.

AN ESTIMATING EQUATION IN CHILDREN

GFR Estimation in Children: The CH Study

An estimating equation for estimating GFR in children was created, which takes into account both age and gender, improving the accuracy of the estimation.

References


Additional information and resources are available at the National Kidney Foundation website.
There are many formulae that can be used to estimate GFR. Currently, the CKD-EPI cystatin C equation not adjusted for age, sex, and race14:

\[ \text{egfr} = 76.7 \times \text{CysC} \]

is recommended for the general population. In African Americans who are female, the age-adjusted equation is:

\[ \text{egfr} = 186 \times \text{sCr} - 1.154 \times \text{age} - 0.203 \]

or for age, sex, and race15:

\[ \text{egfr} = 78.7 \times \text{CysC} - 0.118 \times \text{age} - 0.203 \]

There are other equations for estimating GFR that are adjusted for age, sex, and race. In children, a new equation is available:

\[ \text{egfr} = \frac{3.12 \times \text{height (m)}}{\text{Scr (mg/dl)}} \]

This equation is based on the Swiss Pediatric Study Group, which compared cystatin C and serum creatinine levels in children. The cystatin C equation was found to be more accurate in predicting GFR in children compared to the serum creatinine equation.

In adults, the cystatin C equation can be used to estimate GFR:

\[ \text{egfr} = 186 \times \text{sCr} - 1.154 \times \text{age} - 0.203 \]

The cystatin C equation is more accurate in predicting GFR compared to the serum creatinine equation, especially in older adults and in individuals with a low GFR.

In conclusion, the cystatin C equation is a valuable tool for estimating GFR in adults and children. It is recommended for use in clinical practice and research.
cystatin C equations

1. The original MDRD study equation:
   \[ \text{GFR (ml/min/1.73 m^2)} = \left( \frac{175}{\text{serum creatinine}} \right) \times 0.742 \]

2. The "reexpressed" MDRD study equation:
   \[ \text{GFR (ml/min/1.73 m^2)} = \left( \frac{175}{\text{serum creatinine}} \right) \times 1.212 \]

3. The cystatin C equation:
   \[ \text{GFR (ml/min/1.73 m^2)} = \left( \frac{175}{\text{serum cystatin C}} \right) \times 0.742 \]

4. For standardized SCR:
   \[ \text{GFR (ml/min/1.73 m^2)} = \left( \frac{175}{\text{serum cystatin C}} \right) \times 1.06 \]

Bias, precision, and accuracy

- **Bias:** Difference between the estimated and true GFR.
- **Precision:** Consistency of the estimates.
- **Accuracy:** Proportion of estimates falling within a specified range of the true GFR.

Multiple factors influence these metrics, including the method of measurement (e.g., cystatin C vs. creatinine) and the population studied.

Guidance for comparing GFR predicting equations

When comparing different GFR predicting equations, it is important to consider:
- The population studied: Differences may exist between studies due to variations in demographic and clinical characteristics.
- The method of measurement: Different methods may yield different results, necessitating a clear comparison of methodologies.
- The clinical context: The relevance of a particular equation may vary depending on the clinical setting (e.g., in children, elderly patients, or specific patient groups).

Using Cystatin C: Clinical Considerations with Certain Diagnoses

Cardiovascular Disease

- **Pathophysiology:** Elevated cystatin C in cardiovascular disease reflects increased myocardial and vascular stress, possibly due to fibrosis and inflammation.
- **Clinical Implications:** Cystatin C may serve as a biomarker for heart failure, predicting mortality, and guiding treatment decisions.

Glomerular Disease

- **Pathophysiology:** Cystatin C may be increased in glomerular disease due to enhanced production or reduced clearance.
- **Clinical Implications:** Cystatin C can help in the early detection and monitoring of kidney disease.

Hepatic Disease

- **Pathophysiology:** Cystatin C is produced in the liver and its levels can be influenced by hepatic function.
- **Clinical Implications:** Elevated cystatin C in hepatic disease may reflect liver damage or dysfunction.

GFR Estimation in Children: The CKD Study

- **Adjustment for Age:** Equations for children may need to be adjusted for age, sex, and weight to account for differences in renal function development.
- **Methodological Considerations:** The choice of equation may depend on the age group and the presence of comorbidities.

Additional references and resources are provided at the end of the document.
There are many formulae that can be used to estimate GFR. Currently, the most widely used methods are the Cockcroft-Gault equation and the Modification of Diet in Renal Disease (MDRD) study equation. The Cockcroft-Gault equation is:

\[
\text{eGFR} = \frac{141 \times \text{serum creatinine}}{\text{body weight (kg)} \times 0.85^{\text{if female}}}
\]

The MDRD study equation is:

\[
\text{eGFR} = \frac{186 \times \text{serum creatinine}^{1.154} \times \text{age}^{0.203} \times 0.742 \text{ if African American}}{1.21 \times \text{if not white}}
\]

There are also other equations that can be used, such as the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation:

\[
\text{eGFR} = \frac{141 \times \text{serum creatinine}^{1.209} \times \text{age}^{0.203} \times 0.742 \text{ if African American}}{1.21 \times \text{if not white}}
\]

The CKD-EPI equation is more accurate for people with a creatinine concentration of 1.0 mg/dL or lower, while the MDRD study equation is more accurate for people with a creatinine concentration of 1.0 mg/dL or higher.

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