Overview

Useful For
Creatinine:
- Diagnosing and monitoring treatment of acute and chronic renal diseases
- Adjusting dosage of renally excreted medications
- Monitoring renal transplant recipients

Estimated Glomerular Filtration Rate (eGFR):
Serum creatinine measurement is used in estimating GFR for people with chronic kidney disease (CKD) and those with risk factors for CKD (diabetes, hypertension, cardiovascular disease, and family history of kidney disease)

Method Name
Enzymatic Colorimetric Assay

NY State Available
Yes

Specimen

Specimen Type
Serum

Necessary Information
Patient's age and sex are required.

Specimen Required

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 0.5 mL

Collection Instructions:
1. Serum gel tubes should be centrifuged within 2 hours of collection.
2. Red-top tubes should be centrifuged and aliquoted within 2 hours of collection.

Forms
If not ordering electronically, complete, print, and send a Renal Diagnostics Test Request (T830) with the specimen.

Specimen Minimum Volume
Test Definition: CRTS1
Creatinine with eGFR, S

0.25 mL

Reject Due To

<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>Reject</th>
</tr>
</thead>
</table>

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>7 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>90 days</td>
<td></td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information

Creatinine:

In muscle metabolism, creatinine is synthesized endogenously from creatine and creatine phosphate. Creatinine is removed from plasma by glomerular filtration into the urine without being reabsorbed by the tubules to any significant extent. Renal tubular secretion also contributes a small quantity of creatinine to the urine. As a result, creatinine clearance often overestimates the true glomerular filtration rate (GFR) by 10% to more than 20%.

Determinations of creatinine and renal clearance of creatinine are of value in the assessment of kidney function. Serum or blood creatinine levels in renal disease generally do not increase until renal function is substantially impaired.

Estimated glomerular filtration rate (eGFR):

eGFR is calculated using the 2009 chronic kidney disease (CKD) epidemiology collaboration (CKD-EPI) equation:

\[
eGFR \text{ (CKD-EPI)} = 141 \times \min(\text{Scr}/k, 1) \alpha \times \max(\text{Scr}/k, 1) - 1.209 \times 0.993 \text{age} \times 1.018 \text{ (if patient is female)} \times 1.159 \text{ (if patient is black)}
\]

- where age is in years
- k is 0.7 for females and 0.9 for males
- \(\alpha\) is -0.329 for females and -0.411 for males
- \(\min\) indicates the minimum of Scr/k or 1
- \(\max\) indicates the maximum of Scr/k or 1.

Use of an estimating or prediction equation to estimate GFR from serum creatinine should be employed for people with CKD and those with risk factors for CKD (diabetes, hypertension, cardiovascular disease, and family history of kidney disease). Reasons given for routine reporting of eGFR with every serum creatinine in adult (18 and over) patients include:
-GFR and creatinine clearance are poorly inferred from serum creatinine alone. GFR and creatinine clearance are inversely and nonlinearly related to serum creatinine. The effects of age, sex, and, to a lesser extent, race, on creatinine production further cloud interpretation.

-Creatinine is commonly measured in routine clinical practice. Albuminuria (>30 mg/24 hour or urine albumin to creatinine ratio >30mg/g) may be a more sensitive marker of early renal disease, especially among patients with diabetic nephropathy. However, there is poor adherence to guidelines that suggest annual urinary albumin testing of patients with known diabetes. Therefore, if a depressed eGFR is calculated from a serum creatinine measurement, it may help providers recognize early CKD and pursue appropriate follow-up testing and therapeutic intervention.

-Monitoring of kidney function (by GFR or creatinine clearance) is essential once albuminuria is discovered. Estimated GFR is a more practical means to closely follow changes in GFR over time, when compared to direct measurement using methods such as iothalamate clearance.

-The CKD-EPI equation does not require weight or height variables. From a serum creatinine measurement, it generates a GFR result normalized to a standard body surface area (1.73 m\(^2\)) using sex, age, and race. Unlike the Cockcroft-Gault equation, height and weight, which are often not available in the laboratory information system, are not required. The CKD-EPI equation does require race (African American or non-African American), which also may not be readily available. For this reason, eGFR values for both African Americans and non-African Americans are reported. The difference between the 2 estimates is typically about 20%. The patient or provider can decide which result is appropriate for a given patient.

The Kidney Disease: Improving Global Outcomes (KDIGO) CKD work group clinical practice guideline,(2) as further defined by the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) commentary,(3) provide the following recommendations for reporting and interpretation of serum creatinine and eGFR:

1.4.3: Evaluation of GFR

-1.4.3.1: We recommend using serum creatinine and a GFR estimating equation for initial assessment. (1A)

1.4.3.2: We suggest using additional tests (such as cystatin C or a clearance measurement) for confirmatory testing in specific circumstances when eGFR based on serum creatinine is less accurate. (2B)

1.4.3.3: We recommend that clinicians (1B):

-Use a GFR estimating equation to derive GFR from serum creatinine (eGFRcreat) rather than relying on the serum creatinine concentration alone.

-Understand clinical settings in which eGFRcreat is less accurate.

1.4.3.4: We recommend that clinical laboratories should (1B):

-Measure serum creatinine using a specific assay with calibration traceable to the international standard reference materials and minimal bias compared to isotope-dilution mass spectrometry (IDMS) reference methodology.

-Report eGFRcreat in addition to the serum creatinine concentration in adults and specify the equation used whenever reporting eGFRcreat.

-Report eGFRcreat in adults using the 2009 CKD-EPI creatinine equation. An alternative creatinine-based GFR estimating equation is acceptable if it has been shown to improve accuracy of GFR estimates compared to the
2009 CKD-EPI creatinine equation.

When reporting serum creatinine:

- We recommend that serum creatinine concentration be reported and rounded to the nearest whole number when expressed as standard international units (mmol/l) and rounded to the nearest 100th of a whole number when expressed as conventional units (mg/dl).

When reporting eGFRcreat:

- We recommend that eGFRcreat should be reported and rounded to the nearest whole number and relative to a body surface area of 1.73 m2 in adults using the units ml/min/1.73 m2.
- We recommend eGFRcreat levels less than 60 ml/min/1.73 m2 should be reported as "decreased".

1.4.3.8: We suggest measuring GFR using an exogenous filtration marker under circumstances where more accurate ascertainment of GFR will impact treatment decisions (2B)

**Reference Values**

**CREATININE**

**Males** (1)

0-11 months: 0.17-0.42 mg/dL

1-5 years: 0.19-0.49 mg/dL

6-10 years: 0.26-0.61 mg/dL

11-14 years: 0.35-0.86 mg/dL

> or =15 years: 0.74-1.35 mg/dL (2)

**Females** (1)

0-11 months: 0.17-0.42 mg/dL

1-5 years: 0.19-0.49 mg/dL

6-10 years: 0.26-0.61 mg/dL

11-15 years: 0.35-0.86 mg/dL

> or =16 years: 0.59-1.04 mg/dL (2)

**ESTIMATED GFR**

> or =60 mL/min/BSA

**Note**: eGFR results will not be calculated for patients <18 years old.
Interpretation

Creatinine:

Because serum creatinine is inversely correlated with glomerular filtration rate (GFR), when renal function is near normal, absolute changes in serum creatinine reflect larger changes than do similar absolute changes when renal function is poor. For example, an increase in serum creatinine from 1 to 2 mg/dL may indicate a decrease in GFR of 50 mL/min (from 100 to 50 mL/min), whereas an increase in serum creatinine level from 4 to 5 mg/dL may indicate a decrease of only 5 mL/min (from 25 to 20 mL/min).

Because of the imprecision of serum creatinine as an assessment of GFR, there may be clinical situations where a more accurate GFR assessment must be performed, iothalamate or inulin clearance are superior to serum creatinine and eGFR.

Several factors may influence serum creatinine independent of changes in GFR. For instance, creatinine generation is dependent upon muscle mass. Thus, young, muscular males may have significantly higher serum creatinine levels than elderly females, despite having similar GFRs. Also, because some renal clearance of creatinine is due to tubular secretion, drugs that inhibit this secretory component (eg, cimetidine and trimethoprim) may cause small increases in serum creatinine without an actual decrease in GFR.

Estimated GFR:

According to the Kidney Disease: Improving Global Outcomes (KDIGO) CKD work group, chronic kidney disease (CKD) is defined as the abnormalities of kidney structure or function, present for more than 3 months, with implications for health.(3,4) CKD should be classified by cause, GFR category, and albuminuria category.(3,4) KDIGO guidelines provide the following GFR categories(2,3):

<table>
<thead>
<tr>
<th>Stage</th>
<th>Terms</th>
<th>GFR mL/min/1.73 m(4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1*</td>
<td>Normal or high</td>
<td>90</td>
</tr>
<tr>
<td>G2*</td>
<td>Mildly decreased</td>
<td>60 to 89</td>
</tr>
<tr>
<td>G3a</td>
<td>Mildly to moderately decreased</td>
<td>45 to 59</td>
</tr>
<tr>
<td>G3b</td>
<td>Moderately to severely decreased</td>
<td>30-44</td>
</tr>
<tr>
<td>G4</td>
<td>Severely decreased</td>
<td>15-29</td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

*In the absence of evidence of kidney damage, neither G1 nor G2 fulfill criteria for CKD.

Cautions

Creatinine:

-Ascorbic acid: less than 1.70 mmol/L or less than 300 mg/dL does not interfere.

-No interference was found at therapeutic concentrations using common drug panels. Exceptions: Rifampicin, Levodopa and calcium dobesilate (Dexium) cause artificially low creatinine results. Dicynone (Etamsylate) at
therapeutic concentrations may lead to falsely low results.

-N-Ethylglycine at therapeutic concentrations and DL-proline at concentrations greater than or equal to 1 mmol/L give falsely high results.

-No significant interference up to creatine level of 4 mmol/L (524 mg/L).

-Hemolyzed specimens from patients with hemoglobin F (Hbg F) values of 600 mg/dL and higher interfere with the test.

-2-Phenyl-1,3-indandion (phenindion) at therapeutic concentrations interferes with the assay.

-In patients receiving catecholamines (dopamine, dobutamine, epinephrine, and norepinephrine) falsely low results might be observed.(5)

-Acetaminophen intoxications are frequently treated with N-acetylcysteine. N-Acetylcysteine at the therapeutic concentration of 3.4 mmol/L and the acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low creatinine results.

-Venipuncture should be performed prior to the administration of metamizole. Venipuncture immediately after or during the administration of metamizole may lead to falsely low results. A significant interference may occur at any plasma metamizole concentration.

-In very rare cases of gammopathy, in particular Waldenstrom macroglobulinemia (type IgM) may cause unreliable results.

The following do not interfere with this assay:

-Ketone bodies

-Cephalosporin antibiotics

**Clinical Reference**


4. CCL validation study xxyy20163


**Performance**

**Method Description**

Creatinine:
Test Definition: CRTS1
Creatinine with eGFR, S

The enzymatic method is based on the determination of sarcosine from creatinine with the aid of creatinase, creatinase, and sarcosine oxidase. The liberated hydrogen peroxide is measured via a modified Trinder reaction using a colorimetric indicator. Optimization of the buffer system and the colorimetric indicator enables the creatinine concentration to be quantified both precisely and specifically. (Package insert: Roche Cobas creatinine reagent, Roche Diagnostics, Indianapolis IN 12/2016)

Estimated Glomerular Filtration Rate (eGFR):

2009 CKD-EPI creatinine equation:

Black calculation (> or =18 years only):

Females:
If creatinine < or =0.7 mg/dL: 166 x (creatinine/0.7)(-0.329) x 0.993 Age
If creatinine >0.7 mg/dL: 166 x (creatinine/0.7)(-1.209) x 0.993 Age

Males:
If creatinine < or =0.9 mg/dL: 163 x (creatinine/0.9)(-0.411) x 0.993 Age
If creatinine >0.9 mg/dL: 163 x (creatinine/0.9)(-1.209) x 0.993 Age

Non-black calculation (> or =18 years only):

Females:
If creatinine < or =0.7 mg/dL: 144 x (creatinine/0.7)(-0.329) x 0.993 Age
If creatinine < or =0.7 mg/dL: 144 x (creatinine/0.7)(-1.209) x 0.993 Age

Males:
If creatinine < or =0.9 mg/dL: 141 x (creatinine/0.9)(-0.411) x 0.993 Age
If creatinine < or =0.9 mg/dL: 141 x (creatinine/0.9)(-1.209) x 0.993 Age

Values are reported for calculated GFR estimates between 15-90 mL/min/1.73 m². Estimated GFR values outside of this range are reported as "<15 mL/min/1.73 m²" or ">90 mL/min/1.73 m²" and not as an exact number.

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Sunday; Continuously

Analytic Time
Same day/1 day

Maximum Laboratory Time
2 days
Specimen Retention Time
1 week

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test has been cleared or approved by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
82565

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRTS1</td>
<td>Creatinine with eGFR, S</td>
<td>45066-8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRTSA</td>
<td>Creatinine, S</td>
<td>2160-0</td>
</tr>
<tr>
<td>EGNB</td>
<td>eGFR-Non Black</td>
<td>88294-4</td>
</tr>
<tr>
<td>EGBL</td>
<td>eGFR-Black</td>
<td>88293-6</td>
</tr>
</tbody>
</table>