MEASUREMENT OF GLOMERULAR FILTRATION RATE BY EXOGENOUS AND ENDOGENOUS FILTRATION MARKERS

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ABSTRACT: The National Kidney Foundation (NKF), through its Kidney Disease Outcomes Quality Initiative (K/DOQI), and other National institutions proposed glomerular filtration rate (GFR) to describe, classify, screen and examine chronic kidney disease (CKD). GFR is the standard measure of renal function but cannot be practically measured for clinical and research purposes, so serum creatinine (Scr) is used to calculate estimated GFR (eGFR) which is affected by age, weight, muscle mass, race, various medications and extra-glomerular elimination. To overcome this Cystatin C (CysC) is new and reliable marker for renal function due to its low molecular weight it is freely filtered through glomerulus, completely reabsorbed and catabolized, but not secreted, by tubular cells. Various equations used for GFR estimation such as the Modification of Diet in Renal Disease (MDRD) Study equation, Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and Cockcroft–Gault (CG) equation based on Scr, Grubb and Hoek equation based on CysC and Stevens equation based on both SCR and CysC are used. CKD–EPI is preferred for identifying patients with CKD and for staging the disease. The risk of underestimation of kidney function with MDRD is highest when the GFR is 30 mL/minute/1.73 m² so GFR is calculated by CKD–EPI equation for these persons. CKD–EPI is recommended for diagnosis and staging when the addition of appropriate prophylactic drugs or avoidance of certain nephrotoxic drugs should occur.

The aim of this review is to evaluate from recent literature available different exogenous and endogenous markers used for the determination of GFR and which marker found suitable for the determination of GFR according to literature available on PubMed and determine their reliability in the detection and monitoring of CKD and its stages.

Key words: Glomerular filtration rate, chronic kidney disease, Creatinine, Cystatin C, Measurement of GFR

Abbreviations - Glomerular filtration rate (GFR), chronic kidney disease (CKD), Modification of Diet in Renal Disease (MDRD), Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), Cockcroft–Gault (CG), Serum creatinine (Scr), serum cystatin C (CysC), National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (KDOQI), Cardiovascular disease (CVD), Food and drug administration (FDA), Diethylene triamine pentaacetic acid (DTPA), Ethylene diamine tetra acetic acid (EDTA)

INTRODUCTION

The GFR is the best indicator of renal function (Grubb et al., 2005). By definition, GFR is the rate at which substances are filtered from the blood, of the glomeruli into Bowman’s capsules of the nephrons. Early stages of renal function impairment are clinically silent and are diagnosed only by measuring GFR by external filtration markers (measured GFR, mGFR) (Coresh et al., 2005) When GFR <60, functional impairments is detected by internal filtration markers and calculated eGFR (Stevens et al., 2008). The complications of CKD increase with decreasing GFR and may progress from gradual reduction in renal function to end-stage renal disease (ESRD). Low GFR is risk factor for cardiovascular disease (CVD) mortality (Matsushita et al., 2010; Levey et al., 2011). Appropriate dosing of drugs excreted by the kidney is usually based on GFR so GFR is the best marker for assessing the overall function of the kidney (Toto et al., 1995)

Measurement of Glomerular Filtration Rate

GFR cannot be measured directly in humans. It has to be determined indirectly by measuring the clearance of an ideal filtration marker. Such marker has to be freely filtered at the level of the glomerulus so the molecular weight of such a marker has to be low and the compound must not bind to plasma proteins. The ideal marker must be able to achieve a stable plasma concentration, should not be reabsorbed, secreted or metabolized by the kidney, should be physiologically inert and should not alter renal function. Several methods used to measure GFR involve the measurement of ability of the kidney to clear an exogenous or endogenous marker.
Renal clearance of a substance is defined as the volume of plasma from which the substance is completely cleared by the kidneys per unit of time. Depicted as GFR = (US × V) / PS, where GFR = the flow rate in milliliters per minute of plasma through the glomerular membranes. US = Urinary concentration of the substance, V = Volumetric flow rate of urine in milliliters per minute, PS = Plasma concentration of the substance

Renal clearance techniques involve measuring blood and urine concentrations of either endogenous or exogenous substances. GFR is best determined under standardized conditions, which include discontinuation of medication, prior fasting, sufficient water loading to maintain a urine flow rate >1 mL/min, and complete bladder emptying because GFR deviate from normal values for age from various influences including diet, postural changes, alterations in renal nervous tone, hormones, prostaglandins, atrial natriuretic peptide, drugs, pregnancy, and renal diseases. Determination of mGFR and eGFR is useful to measure renal function in patients with high prevalence of GFR <60, staging of CKD into stages I–V and the usefulness of function-preserving treatment measures.

**EXOGENOUS FILTRATION MARKERS (m GFR)** -

**Radio isotopic Markers**

These markers include $^{51}$Cr-ethylenediaminetetraacetic acid (EDTA) (Askergren et al., 1981; Blake et al., 1997; Brochner-Mortensen et al., 1969; Chantler et al., 1972), $^{99}$Tc, diethylenetriaminepentaacetic acid (DTPA), and $^{125}$Iothalamate. $^{51}$Cr-EDTA is best marker as compare to $^{99}$Tc-DTPA and $^{125}$I-iothalamate because its clearance is closest to inulin clearance (Brochner-Mortensen et al., 1969 ; Blaufox et al., 1996). When GFR is measured using urinary or plasma clearance methods, it is essential that renal tubular secretion or reabsorption does not contribute to elimination of the compound, plasma protein binding of the radioisotopic markers is negligible, and no extra-renal elimination of the marker occurs. In patients with low GFR (<30 mL/min) and in patients with ascites or edema, best preferred method is renal clearance method ( Blaufox et al.,1996).

**Non radiosotopic Markers**

Nonradioactive compounds inulin and iohexol (Effersoe et al., 1990) is used to measure GFR. Inulin clearance used as gold standard measure of GFR (Van Rossum et al., 2003) because it is freely filtered by the glomerulus, not reabsorbed, secreted, or metabolized by the renal tubule, not bound to plasma proteins, nontoxic, and physiologically inert, but it requires continuous intravenous infusion; multiple timed urine collections and its measurement is expensive so it is only used in research studies when very accurate estimation of renal function is required.

In Iohexol Clearance non radio labelled iodinated contrast agent, iohexol is used and measured by HPLC with reversed-phase separation and UV detection, following prior deproteinization with perchloric acid (Krutzen et al., 1984). This method is again very expensive and time consuming (Brown et al., 1991; Gaspari et al., 1998; Arvidsson et al., 1990 ; Krutzen et al., 1984). So a new technique is proposed based on X-ray fluorescence, but this method is less sensitive than HPLC and requires administration of significantly larger doses of iohexol, leading to higher risk of nephrotoxicity and adverse reactions (Brown et al., 1991; Gaspari et al., 1998; Rocco et al., 1996).

**Endogenous filtration markers**

Creatinine and low molecular weight proteins cystatin C have been used as endogenous markers of GFR. Most widely used endogenous markers of GFR is Creatinine expressed as its serum concentration or as renal clearance (Rehberg et al., 1926) based on the renal clearance of exogenously administered creatinine. In 1937 the use of endogenous creatinine clearance was developed. (Popper et al., 1937)

**Creatinine**

GFR is determined by measuring Scr which is freely filtered at the glomerulus and its concentration is inversely proportional to the GFR, so that each halving of the GFR results in a doubling of the Scr concentration (Kassirer et al., 1971). Creatinine having molecular mass 113 Da, is a near perfect filtration marker and this is measured by standardized method based on modified jaffe’s reaction which is able to separate Creatinine from non-creatinine chromogens (e.g. acetic acid, acetone, pyruvate, glucose, ascorbic acid, bilirubin) (Tomlinson et al., 1969 ; Horber et al., 1985). The ratio of creatinine clearance to inulin clearance ranges from 1.1 to 1.4 (Smith, 1951; Shannon, 1935; Dodge et al., 1928; Shemesh et al., 1985; Levey et al., 1988). In severe renal insufficiency patients the ratio may reach 2.5, indicates as much as 60% of urinary creatinine is derived from tubular secretion. GFR will deviate from normal value which is 130 mL/mm/1.73 m$^2$ of body surface area in men and 120 mL/min/1.73 m$^2$ in women under the age of 30 years and declines with age there after (Wesson, 1969; Matsushita et al., 2010).

**Creatinine Clearance.**

Creatinine is endogenously produced and released into body fluids at a constant rate, its clearance can be measured and is an indicator of GFR (Perrone et al., 1992). Creatinine clearance in the past has been seen as more sensitive for detection of renal dysfunction than serum creatinine measurement but it requires timed urine collection, which is laborious and inconvenient (Goldberg et al., 1987; Payne, 1986; Ricos et al., 1994) Also Creatinine clearance provide only crude index of GFR.

$$\text{CrCl (mL/min)} = \frac{[\text{Urinary creatinine (mg/dL)} \times \text{urine volume (mL/min)}]}{[\text{SCr (mg/dL)}]}$$
Cystatin C and other low molecular weight protein-
Several low molecular weight proteins of <30 KDa like α2-microglobulin, RBP (Retinol binding protein), α1-
microglobulin, β-trace protein, (Priem et al., 1999) and CysC are freely filtered from circulation by renal filtration,
then reabsorbed in the proximal tubule or excreted into the urine so these are used as a marker of GFR. But their
serum concentrations are influenced by other, non renal factors such as inflammation (α2-microglobulin) and liver
disease (RBP, α1-microglobulin) (Ayatse et al., 1991).

Several groups explained CysC as more sensitive and specific means of monitoring changes in GFR than SCr.
(Finney et al., 1997; Grubb, 1992; Kyhse-Andersen et al., 1994 ; Newman et al., 1995) CysC is a low molecular
weight (12.8 kD) nonglycocylated cationic basic protein consisting of 120 amino acids synthesized by all nucleated
cells belongs to the cystatin superfamily of endogenous cysteine proteinase inhibitors (Pucci et al., 2007; Shlipak et
al., 2005; Risch et al., 2001; Bokenkamp et al., 2002) CysC have small size and high isoelectric point (pI 9.2), which
enable this to freely filtered than other proteins at the glomerulus (Grubb, 1992). Serum concentration of CysC is
unaffected by race, inflammatory conditions, gender, body composition, and age (after 12 months) (Finney et al.,
2000; Bokenkamp et al., 1998) clearance from the circulation occurs only by glomerular filtration (Grubb, 1992;
Jacobsson et al., 1995; Tenstad et al., 1996).

Cys C can be measured by immunodiffusion or rocket electro immunoassay, but these are insensitive methods. Most
practical methods using an automated particle-enhanced turbidimetric immunoassay (PETIA) or nephelometric
immunoassay (PENIA) to measure the formation of antigen-antibody complexes and its reciprocal is highly
practical methods using an automated particle-enhanced turbidimetric immunoassay (PETIA) or nephelometric
immunoassay (PENIA) to measure the formation of antigen-antibody complexes and its reciprocal is highly
Correlated with GFR. Several commercial CysC methods are available including automated applications. CysC was
proposed as a marker of GFR potentially superior to Scr (Dharnidharka et al., 2002). A meta-analysis of 46 cross-
sectional studies including adults and children shows the correlation of GFR with CysC is superior than creatinine
based equation in the estimation of GFR (Brzin et al., 1984). CysC was found to be the best predictor of kidney
failure and death from cardiovascular disease in a longitudinal cohort study of 4637 older people (Simonsen et al.,
1985).

Newman and colleagues found that, in a group of patients with a range of GFRs, the CysC concentration increased
earlier than creatinine as GFR decreased to about 80 mL/min/1.73 m² compared with about 40 mL/min/1.73 m² for
serum creatinine (Newman et al., 1995). CysC was found to be useful to detect mild to moderate impairment of
kidney function (Bostom et al., 2000, Coll et al., 2000).

Advantages and limitations of Cystatin C

Serum concentrations of CysC were found to be unaffected by muscle mass, diet, or gender (Kyhse-Andersen et al.,
1994). Though large doses of glucocorticoids (500 mg methylprednisolone) increased serum CysC concentration,
(Grubb, 1992) low or medium doses of glucocorticoids (20 to 60 mg/day prednisone) have no effect on its
concentration (Bokenkamp et al., 2002). Several publications suggest influence of thyroid hormone (Den Hollander
et al., 2003; Fricker et al., 2003; Jayagopal et al., 2003). CysC levels are lower in the hypothyroid and higher in the
hyperthyroid state as compared with the euthyroid state (Fricker et al., 2003).

Creatinine-based eGFR

Equations for estimating GFR

Various equations used for GFR estimation include the Modification of Diet in Renal Disease (MDRD) (Cockcroft et
al., 1976), the Cockcroft–Gault (CG) (Levey et al., 1999), and the Chronic Kidney Disease Epidemiology
Collaboration (CKD–EPI) (Levey et al., 2009) for adults. In children Schwartz formula was used (Schwartz et al.,
1976).

The CG equation was the first of these three equations developed, which was determined by studying hospitalized
adult male patients (Dharnidharka et al., 2002). The CG equation underestimates GFR in the aged group and is less
accurate in patients which have normal kidney function.

The MDRD equation was the second equation developed in 1999 in chronic renal insufficiency study in which 1,628
men and women were enrolled. This equation was adjusted for 4 variables - body-surface area, race, gender, and age.
GFR is expressed as mL/min/1.73m² and race is categorized as either black or not black.

In the Practice Guidelines for CKD, published in 2002 by the Kidney Disease Outcomes Quality Initiative of the
National Kidney Foundation (K/DOQI) and the more recent Kidney Disease: Improving Global Outcomes (KDIGO)
guidelines simplified MDRD equation has been included as the primary GFR marker and staging of CKD (Levey et
al., 2005; Levey et al., 2011). Most studies confirmed that the MDRD equation provides a more accurate assessment
of GFR than the CG equation (Froissart et al., 2005; Poggio et al., 2005) including among diabetic patients with moderate
to severe CKD (Rigalleau et al., 2005). Limitations of MDRD equation is that at higher values of GFR, it shows
significant negative bias (Poggio et al., 2005 ; Rule et al., 2004) and poor precision (Poggio et al., 2005). New CKD-
EPI equation was developed in 2009 from data of 8254 people with and without CKD in 10 studies and authenticated
in 3896 people in 16 separate populations (Levey et al., 2009). In younger people, whites and women the CKD-EPI
equation gives higher values of eGFR compared with the MDRD equation, at this range the CKD-EPI equation was
more accurate than the MDRD equation (Rule et al., 2004; Levey et al., 2009).
The CKD–EPI equation is standardized for race, Body Surface Area, age and sex and is expressed as mL/min/1.73 m$^2$. In 2002 the National Kidney Foundation’s KDOQI classified CKD on the basis of eGFR. According to this CKD occurs when eGFR < 60 mL/min/1.73m$^2$ for ≥3 months. CKD stages are classified into Stages I–V according to the eGFR as follows: Stage 1 GFR > 90 mL/min/1.73 m$^2$, Stage 2 GFR 60–89 ml/min/1.73 m$^2$, Stage 3 GFR 30–59 ml/min/1.73 m$^2$, Stage 4 GFR 15–29 ml/min/1.73m$^2$ and Stage 5 GFR < 15 ml/ min/1.73 m$^2$.

Table 1 - Classification of stages of chronic kidney disease according to K/DOQI guidelines.

<table>
<thead>
<tr>
<th>Stages of kidney disease</th>
<th>GFR(mL/min/1.73 m$^2$)</th>
<th>Description</th>
<th>Related abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&gt; 90</td>
<td>Healthy kidney</td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>&gt; 90</td>
<td>Normal kidney function</td>
<td>Albuminuria, proteinuria, hematuria</td>
</tr>
<tr>
<td>Stage 2</td>
<td>89-60</td>
<td>Mildly reduced kidney function</td>
<td>Albuminuria, proteinuria, hematuria</td>
</tr>
<tr>
<td>Stage 3 A 3 B</td>
<td>59-45 44-30</td>
<td>Moderately reduced kidney function</td>
<td>Proteinuria, hematuria, anemia, hypocalcemia, hyperphosphatemia</td>
</tr>
<tr>
<td>Stage 4</td>
<td>29-15</td>
<td>Severely reduced kidney function</td>
<td>Proteinuria, hematuria, anemia, acidosis, hypocalcemia, hyperphosphatemia</td>
</tr>
<tr>
<td>Stage 5</td>
<td>&lt;15 or dialysis</td>
<td>Very severe or end stage kidney failure</td>
<td>Uremia, anemia, malnutrition, hyperparathyroidism, high B.P., swelling in hands/legs eyes/lower back, shortness of breath</td>
</tr>
</tbody>
</table>

Table 2 - Creatinine- and Cystatin C-based equations for calculation of eGFR

<table>
<thead>
<tr>
<th>Children</th>
<th>Creatinine-based</th>
<th>Cystatin C-based</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric Schwartz equation (Schwartz et al.,1976)</td>
<td>GFR (ml/min/1.73 m$^2$) = (0.41× height, cm)/ (serum creatinine, mg/dl).</td>
<td>eGFR (mL /min) = 0.43 × height (cm) × (S$_{Cr}$ mg/dL)$^{-1}$</td>
</tr>
<tr>
<td>Counahan-Barratt equation (Counahan et al., 1976)</td>
<td>eGFR (mL /min) = 0.43 × height (cm) × (S$_{Cr}$ mg/dL)$^{-1}$</td>
<td>Cystatin C-based</td>
</tr>
<tr>
<td>Equation according to Grubb et al. (Grubb et al., 2005)</td>
<td>eGFR (mL /min/1.73 m$^2$) = 84.69 × (S$_{cystatin}$ C [mg / L])$^{-1.68}$ × 1.384 (in children &lt;14 years)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adults</th>
<th>Creatinine-based</th>
<th>Cystatin C-based</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cockcroft-Gault equation (Levey et al., 1999)</td>
<td>C$<em>{Cr}$ (mL / min) = (140 – age [years]) × (S$</em>{Cr}$ [mg / dL])$^{-1}$ × (BW [kg] × [72]$^{-1}$)</td>
<td>eGFR (mL / min/1.73 m$^2$) = 175 × (S$_{Cr}$ standardized [mg / dL])$^{-1.154}$ × (age [years]$^{-0.203}$)</td>
</tr>
<tr>
<td>Correction factor: for women × 0.85</td>
<td>Correction factor: for women × 0.742 for blacks × 1.18</td>
<td></td>
</tr>
<tr>
<td>MDRD equation (Stevens et al., 2008)</td>
<td>eGFR (mL / min/1.73 m$^2$) = 177.6 × SCr$^{-0.65}$ x CysC$^{0.7}$ × age$^{-0.20}$ x 0.82 (if female) x 1.11 (if black)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>eGFR_CKDEPI (Levey et al.,2009)</th>
<th>Serum Creatinine [S$_{cr}$] in mg/dl based</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>If Serum Creatinine ≤ 0.7mg/dl</td>
</tr>
<tr>
<td>GFR =166 × (S$_{cr}$/0.7)$^{0.329}$ × (0.993)$^{Age}$</td>
<td></td>
</tr>
<tr>
<td>If Serum Creatinine ≥ 0.7mg/dl</td>
<td></td>
</tr>
<tr>
<td>GFR =166 × (S$_{cr}$/0.7)$^{1.20}$ × (0.993)$^{Age}$</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>If Serum Creatinine ≤ 0.9mg/dl</td>
</tr>
<tr>
<td>GFR =163 × (S$_{cr}$/0.9)$^{0.411}$ × (0.993)$^{Age}$</td>
<td></td>
</tr>
<tr>
<td>If Serum Creatinine ≥ 0.9mg/dl</td>
<td></td>
</tr>
<tr>
<td>GFR =163 × (S$_{cr}$/0.9)$^{1.20}$ × (0.993)$^{Age}$</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Equation according to Hoek et al., (2003)</th>
<th>Cystatin C-based</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR (mL/min/1.73 m$^2$) = 80.35 × (S$_{cystatin}$ C [mg / L] – 4)$^{-1.68}$</td>
<td></td>
</tr>
</tbody>
</table>

| Stevens et al ., (2008) |
|-------------------------|---|
| GFR = 177.6 × SCr$^{-0.65}$ x CysC$^{0.7}$ × age$^{-0.20}$ x 0.82 (if female) x 1.11 (if black) |
Estimating GFR for medication adjustment

NKF and the American College of Cardiology (ACC)/American Heart Association (AHA) (Braunwald et al., 2002) approved CG equation for dose-adjusting medications based on kidney function. NKF recommends that MDRD unadjusted for BSA (not multiplying MDRD by the patient’s BSA) is a method for adjusting medication doses based on kidney function. In 1998 FDA Guidance for Industry document suggest CG for drug labelling recommendations. A study of 5,000 subjects found that MDRD adjusted for BSA correctly identified dose reductions 88% of the times, and the CG equation accurately calculated the renal dose adjustments 85% and 82% of the times, using actual and ideal body weights, respectively (Stevens et al., 2009).

Benefits and limitations of the MDRD equation

Advantages of the MDRD equation when compared with nuclear medicine techniques, which are considered as the gold standard for kidney function measurement, creatinine or urea clearance is that the formula was more accurate and this equation does not require 24-hour urine collection, which is inconvenient for patients yielding false positives for CKD. Limitations of this equation is that it cannot evaluated in persons <18 years and >75 years of age, pregnant women, extremes in body size and races other than Caucasian and African American. MDRD equation was not suitable in normal renal function type I diabetes, elderly, and kidney transplant recipients (Norden et al., 1987; Waz et al., 1993; Stoves et al., 2002).

Table-3 Standard Markers of Glomerular Filtration Rate

<table>
<thead>
<tr>
<th>Standard</th>
<th>Markers</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gold standard</td>
<td>Inulin</td>
<td>Gold standard</td>
<td>Exogenous, time-consuming (Estelberger et al., 1995). requires timed urine collection Poor specificity of analysis</td>
</tr>
<tr>
<td></td>
<td>continuous-infusion urinary clearance method</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silver standard</td>
<td>Inulin</td>
<td></td>
<td>Exogenous, Time-consuming (Estelberger et al., 1995). Poor specificity of analysis</td>
</tr>
<tr>
<td></td>
<td>single-bolus plasma clearance method</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronze standard</td>
<td>Iohexol</td>
<td>Nonradioisotopic</td>
<td>Exogenous</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>Endogenous, Inexpensive</td>
<td>Poor sensitivity and specificity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Can be used to estimate GFR from equations (e.g., MDRD,CKD-EPI)</td>
<td></td>
</tr>
<tr>
<td>Other markers</td>
<td>Cystatin C</td>
<td>Not secreted and reabsorbed and more sensitive and specific than creatinine</td>
<td>Influence of thyroid function (Den Hollander et al., 2003; Fricker et al., 2003; Jayagopal et al., 2003)</td>
</tr>
<tr>
<td></td>
<td>Creatinine clearance and Urea</td>
<td>Endogenous and Inexpensive</td>
<td>Requires timed urine collection Inaccurate, Poor sensitivity and specificity</td>
</tr>
<tr>
<td></td>
<td>Retinol binding protein (RBP) and α1-Microglobulin</td>
<td>Endogenous Not secreted/reabsorbed</td>
<td>Non renal influences on production rate</td>
</tr>
</tbody>
</table>

Cystatin C-based eGFR

Several groups have recently developed equations to calculate GFR from serum CysC. In comparison with the MDRD equation, which was calculated from a large population in a multicenter study, CysC based equations were created and validated in smaller samples using different gold standard measurements for GFR. CysC based equation for children according to Grubb (Grubb et al., 2005) has proved more reliable than the Counahan-Barratt equation (Counahan et al., 1976) and for adults Hoek equation (Hoek et al., 2003) is more sensitive than the MDRD equation. In older age groups the physiological decrease in GFR from year to year is listed more sensitively with CysC based eGFR than GFR estimated by the MDRD equation (Shlipak et al., 2009), and GFR >3 is associated with a higher successive risk of mortality (Rifkin et al., 2008).
Recently, (Stevens et al., 2008) developed an equation to estimate eGFR which include both SCr and CysC. Age, gender and race better than earlier equation based on SCr and CysC regarding to bias, precision and accuracy (Rigalleau et al., 2007; Ma et al., 2007, Tidman et al., 2007)

Advantages of Cystatin C based eGFR

CysC based eGFR sensitive for acute as well as chronic kidney disease and this eGFR estimation is independent of age, sex, race, lean muscle mass and diet. In patients having potentially nephrotoxic medications such as contrast media cancer therapeutics or antibiotics in cardiovascular disease patient’s early detection of kidney damage is possible which improves patient’s outcome in renal disease.

CONCLUSIONS

The goal of GFR determination is to diagnose chronic kidney disease in early stages to enable clinicians to slow its progress. GFR is determined by various exogenous and endogenous markers. Exogenous marker such as inulin is gold standard marker of GFR but it is time consuming and required timed urine collection to avoid these endogenous markers based GFR equation introduced which is based on SCr, CysC and both SCr, CysC. Most research studies shows that CKD–EPI is the most accurate method for diagnosis and staging of CKD and CG for drug-dosing decisions. The FDA recommends that CG and MDRD both incorporated into the drug label.

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