eGFR; Whatever next?

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eGFR hits the QoF

GFR = 175 x \((\text{creatinine}(\mu\text{mol/L})-\text{intercept})/\text{slope})\)^{-1.154} x (Age)^{-0.203} x [0.742 if patient is female] x [1.212 if African American]
Renal Bods: - Joy!
“Greatest advance in renal medicine this century”

Lab Bods: - Despair!
“Why didn’t you speak to us first!”

Primary Care: - Confusion!
“Not sure what it means, but we have to have it now!”
Among patients with chronic kidney disease, the stage of disease should be assigned based on the level of kidney function, irrespective of diagnosis, according to the K/DOQI CKD classification:

**Table 10. Stages of Chronic Kidney Disease**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60–89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30–59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 (or dialysis)</td>
</tr>
</tbody>
</table>

- Normal
- Mild
- Moderate impairment
- Severe impairment
- Established renal disease
What to Measure: RCGP

<table>
<thead>
<tr>
<th>CKD stage</th>
<th>Tests</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 and 2</td>
<td>BP eGFR Urine PCR*</td>
<td>yearly</td>
</tr>
<tr>
<td>3</td>
<td>- also Hb, potassium calcium, phosphate</td>
<td>6 monthly (12 if stable **)</td>
</tr>
<tr>
<td>4 and 5</td>
<td>- also bicarbonate, PTH</td>
<td>3 monthly (6 if stable CKD stage 4 **)</td>
</tr>
</tbody>
</table>

* if dipstick protein present  ** stable=<2mL/min change eGFR over 6months
## Problem: Majority of patients with CKD have an eGFR >60 mL/ min/ 1.73m²

Prevalence of CKD: NHANES III Adults >20

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>eGFR MDRD ml/min/1.73m²</th>
<th>Prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>Kidney damage With “normal” GFR</td>
<td>≥ 90</td>
<td>3.3</td>
</tr>
<tr>
<td>2 *</td>
<td>Kidney Damage with mildly ↓ GFR</td>
<td>60-89</td>
<td>3.0</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30-59</td>
<td>4.3</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
<td>0.2</td>
</tr>
<tr>
<td>5</td>
<td>Kidney Failure</td>
<td>&lt;15</td>
<td>0.1</td>
</tr>
</tbody>
</table>

* Albumin/ creatinine ratio 1.9mg/ mmol males; 2.8 mg/ mmol female on 2 occasions.
Problem: Equation not Universally Applicable

- Steak Pie
- Race = Cherub i.e. not white or African American
- Under 18?
- Pregnant or Obese?
- One Leg
- Strenuous Exercise Creatine Supplements
Problems:

- High and variable referral rates due to:
  - inaccuracy of creatinine measurements
  - Uncertainty as to correct course of action in primary care. (e.g. 80 year old lady eGFR = 56 ?)

- Increase in biochemistry workloads.
Where are the Cavalry?

Scotland Forever!  Lady Elizabeth Butler

Royal College of Physicians Edinburgh

Nephrol Dial Transplant. 2007 Sep;22(9):2455-7

Main Changes: -

- Report eGFR as > 60 ml/min/1.73/M\(^2\) across the UK.

- Stage 3 now: -
  - 3A 45 to 59
  - 3B 30 to 44

- Suffix P = proteinuria = PCR 100 mg/mmol creatinine = risk

- If \(\Delta eGFR > 4\) mL/min/1.73M\(^2\) refer?

Proteinuria not in QoF Yet!
Guidance for Labs: -

- Enzymatic creatinine or slope and intercept adjusters

- *Indicate on reports* that an eGFR greater than 60 does not exclude CKD stages 1 and 2; *urinalysis and further investigations where appropriate*

- Report CKD 3a and 3B

- *Provide indicators of the significance of change* between serial results (e.g. reference change value).

- *Provide specific recommendations on collection procedures* to minimise biological and other sources of variation.
Clear Guidance for GPs

Stage 1, 2 and 3A: -
- Manage cardiovascular risk factors
- Annual review with; -
  - eGFR,
  - Urinalysis
  - Blood pressure

Stage 3B
- 6 monthly review as above

Primary aim to reduce progression optimise blood pressure and reduce proteinuria.
Help for Lab workload!

Bone and Mineral Disorders

- Not common in early CKD. Recommend leaving the PTH measurements to the renal units.

Anaemia

- Uncommon unless diabetic or eGFR < 45 mL/min/1.73m²
Problem: eGFR > 60?

- Is it falling at a rate of greater than 4 mL/min/1.73m²/year?

- Creatinine measurement employing appropriate reference intervals and reference change values?
Significance of Change

Reference Change Values?

- eGFR or Creatinine.

- Biological Variation: Average within subject ($CV_1 = 4.3\%$)
Biological Variation

Reference Change Value

- Interpretation of serial results.
- Difference > than combined analytical and biological variation: -

$$RCV = 2^{1/2} \times Z \times (CV_A^2 + CV_I^2)^{1/2}$$

The $Z$ score determines the level of significance of the change: -

e.g. 1 tailed  95% = 1.65
    99% = 2.33
RCV eGFR.

GFR = 175 x (creatinine)$^{-1.154}$ x (Age)$^{-0.203}$ x [0.742 if patient is female] x [1.212 if African American]

Confidence limits?

- Only analytical Variable is the Creatinine with a CV$_i$ of 4.3% the impact of this is increased by the power function in the equation to an average of 5.4%.

- Non linear relationship between eGFR and [Creatinine] = non linear relationship between probability of change and starting eGFR.
"% Probability that % Fall in eGFR is Significant"
Significance of Fall in eGFR at CKD Classification Boundaries

% Probability that Fall is Significant vs. Fall in eGFR in mL/min/1.73m²

- 90 mL
- 60 mL
- 45 mL
- 30 mL
- 15 mL
- 4 mL/min/1.73m²
"% Probability that %Rise in Serum Creatinine is Significant
Observation: -

- The significance of a change depends on starting eGFR
- Single cut off of 4 mL maybe clinically useful, but carries different significance at different levels of eGFR
- Complicated story to tell GPs
Question being Asked?

- Has the patient got reduced renal function?
- Has the function deteriorated?
Answer?

- Use eGFR for initial classification of CKD stage.

- Use creatinine to follow patients with RCV indicator flag?
  - More Precise?
# RCV for eGFR and Creatinine: -

<table>
<thead>
<tr>
<th></th>
<th>% Change at 95%</th>
<th>% Change at 99%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rise in Creatinine</td>
<td>10.3%</td>
<td>14.6%</td>
</tr>
<tr>
<td>Fall in eGFR</td>
<td>12.8%</td>
<td>15.4%</td>
</tr>
</tbody>
</table>

Assumes a $CV_A = 1\%$
$CV_I = 4.3 \%$ creatinine
$CV_I = 5.4 \%$ eGFR
How do we communicate the significance

- Use graphs?
- Report probabilities?
- Flags?
55 year old white male

Creatinine rise from 116 to 128
Change = 10.3%
95% probability of significant rise
eGFR at baseline = 60mL/min/1.73m²
eGFR now = 53 mL/min
Change = 11.6% = 7 mL
93.5% probability significant fall in eGFR
Patient referral?
55 year old White Male

Creatinine rise from 206 to 227
Change = 10.3%
95% probability of significant rise
eGFR at baseline = 30mL/min/1.73m²
eGFR now = 27 mL/min
Change = 10 % = 3 mL
90% probability significant fall in eGFR
Patient referral?
55 year old White Female

Creatinine rise from 206 to 227

Change = 10.3%

95% probability of significant rise

eGFR at baseline = 23 mL/min/1.73m²

eGFR now = 20 mL/min

Change = 10% = 3 mL

90% probability significant fall in eGFR

Patient referral?
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>SODIUM</td>
<td>130 **</td>
<td>135-147</td>
</tr>
<tr>
<td>POTASSIUM</td>
<td>4.0</td>
<td>3.5-5.0</td>
</tr>
<tr>
<td>UREA</td>
<td>28.2 **</td>
<td>3.3-6.6</td>
</tr>
<tr>
<td>CREATININE</td>
<td>212 **</td>
<td>44-80</td>
</tr>
<tr>
<td>ESTIMATED GFR</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>CRF Stage</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>47 **</td>
<td>12-40</td>
</tr>
<tr>
<td>BILIRUBINS</td>
<td>12</td>
<td>0-15</td>
</tr>
<tr>
<td>ALKALINE PHOSPHATASE</td>
<td>50.3 **</td>
<td>20-80</td>
</tr>
<tr>
<td>ALBUMIN</td>
<td>&lt; 34</td>
<td>36-50</td>
</tr>
<tr>
<td>GCT</td>
<td>651 &gt;&gt;</td>
<td>5-35</td>
</tr>
</tbody>
</table>

Lab Comments: Sample Date/Time
18 Aug 2007 07:34

Clin Details: CF, bilateral lung transplant

Request Entered: 18 Aug 2007 09:54
eGFR > 60 in a 30 year old white female: Changing renal function? NB! Change has taken Place within the confines of the reference limits. * indicates significant change
84 year old white male: Stable renal function

> Indicates value above reference interval
eGFR ?
eGFR?