CKD classification: a simple proposal

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Reference intervals for Enzymatic Scr

• White males
  – Q = Median = 0.90 mg/dL
  – URL = 1.16 mg/dL
  – LRL = 0.63 mg/dL
  URL/Median ≈ 1.33
  LRL/Median ≈ 0.67

• White females
  – Q = Median = 0.70 mg/dL
  – URL = 0.93 mg/dL
  – LRL = 0.48 mg/dL
  URL/Median ≈ 1.33
  LRL/Median ≈ 0.67

• Note that Scr/Q = 1 on average, ranging from 0.67 till 1.33

Reference intervals for Enzymatic Scr

- Scr remains constant, on average, during adulthood
- Note the small increase with age of median Scr starting around 65 years

The % of patients with Scr > URL is about 5% for ages between 0 and 60 years, gradually increasing for ages > 65 years.

Criticism on eGFR equations

What’s wrong with using serum creatinine alone?
Criticism on eGFR equations

- Most used eGFR equations (till 2009) are:
  - Cockcroft-Gault equation (for Jaffe type assays)
  - MDRD-equation (2 versions):
    \[ eGFR = 175 \times \text{Scr}^{-1.154} \times \text{Age}^{-0.203} \times 0.742 \text{ (if female)} \times 1.212 \text{ (if Afro American)} \]
  - CKD-EPI
- MDRD equation is not useful for eGFR > 60 ml/min/1.73m² because of its underestimation of the true GFR for healthy people
- MDRD underestimates the true GFR in the elderly (especially in women)
- There is no advantage of using eGFR equations over the use of Scr!!

Current CKD classification system

- Current CKD classification limits
  - Stage I/II: GFR > 60 ml/min/1.73m² but other signs of kidney damage
  - Stage III: GFR < 60 ml/min/1.73m²
  - Stage IV: GFR < 30 ml/min/1.73m²
  - Stage V: GFR < 15 ml/min/1.73m²

- GFR is recommended to be estimated with the MDRD equation
- Since 2010, the CKD-EPI equation is a better alternative
Alternative CKD classification system

- There is little difference between eGFR and Scr
- Data for n = 196513 observations

Alternative classification for CKD

• Current versus alternative classification for CKD
• Example: white males

eGFR equations versus Scr/Q

- eGFR-MDRD can be rewritten in terms of Scr/Q

\[
eGFR = 175 \, \text{Scr}^{-1.154} \, \text{Age}^{-0.203} \, (\times 0.742 \, \text{if female}) \, (\times 1.212 \, \text{if Afro-American})
\]

- With Q = 0.90 mg/dL (white males)
- With Q = 0.70 mg/dL (white females)
- With Q = 1.06 mg/dL (black males)
- With Q = 0.82 mg/dL (black females)

- Note that Scr = Q corresponds to average healthy persons
- When Scr/Q = 1, eGFR is only age-dependent

\[
eGFR = 197(\text{Scr}/\text{Q})^{-1.154} \, \text{Age}^{-0.203}
\]

\[
eGFR = 262(\text{Scr}/\text{Q})^{-1.154} \, \text{Age}^{-0.256}
\]

eGFR equations versus Scr/Q

- eGFR-CKD-EPI can be rewritten in terms of Scr/Q
  
  \[
  \text{eGFR} = 141 \times \min \left( \frac{\text{Scr}}{\kappa}, 1 \right)^\alpha \times \max \left( \frac{\text{Scr}}{\kappa}, 1 \right)^{-1.209 \times (0.993)^{\text{Age}}} \\
  \times (1.018 \text{ if female}) \times (1.159 \text{ if black})
  \]

  - With Q = 0.90 mg/dL (white males)
  - With Q = 0.70 mg/dL (white females)
  - With Q = 1.0125 mg/dL (black males)
  - With Q = 0.7825 mg/dL (black females)

- Note that Scr = Q corresponds to average healthy persons
- When Scr/Q = 1, eGFR is only age-dependent

eGFR equations versus Scr/Q

- eGFR-CKD-EPI can be rewritten in terms of Scr/Q

\[
eGFR = 141 \times \min\left(\frac{Scr}{\kappa}, 1\right)^{\alpha} \times \max(\frac{Scr}{\kappa}, 1)^{-1.209} (0.993)^{Age} \\
\times (1.018 \text{ if female}) \times (1.159 \text{ if black})
\]

\[
eGFR = 142 \times \left(\frac{Scr}{Q}\right)^{-1.234} (0.993)^{Age} \text{ for } Scr / Q > 1
\]

\[
eGFR = 142 \times \left(\frac{Scr}{Q}\right)^{-0.405} (0.993)^{Age} \text{ for } Scr / Q \leq 1
\]

Age-dependency of eGFR

- Age dependency of eGFR-MDRD and eGFR-CKD-EPI
  - Scr/Q = 1.33 (URL)
  - Scr/Q = 1 (av. healthy)
  - Scr/Q = 0.67 (LRL)

CKD classification: a simple proposal

- Based on the fact that Scr/Q is independent of
  - Sex
  - Race
  - Age

- CKD Classification system:
  - Stage I/II: Scr/Q ≤ 1.5
  - Stage III: Scr/Q > 1.5
  - Stage IV: Scr/Q > 2.5
  - Stage V: Scr/Q > 4.5

- Pottel H, Hoste L, Martens M. *Chronic Kidney Disease Classification: A Simple Proposal.* Eur Nephrol (2011); 5:10-14
CKD classification: a simple proposal

- Cutoffs for Scr/Q versus eGFR-CKD-EPI

CKD classification: a simple proposal

- Comparison of CKD classification systems

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- $n = 506$, aged 18-55 years
- $n = 4746$, aged 55-75 years

CKD classification: a simple proposal

- Comparison of CKD classification systems

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- Perfect classification agreement = 96.5%
- Less elderly in class III: 20158 vs 15861 (reduction of 20%)
- More sensitive for young people (n = 506)
- Major differences are in Class I/II and III

CKD classification: what about the elderly?

- CKD prevalence rate (%) for CKD-EPI is influenced by
  - Age dependency of eGFR combined with fixed cutoff values
  - Slightly increasing Scr in the elderly

CKD classification: conclusions

• Scr/Q is simple; no statistical models involved
• Combined with fixed cutoff values: 1.5, 2.5 and 4.5, based on the fact that Scr/Q is constant (independent of age, sex and race)
• Q can be determined as the median of large hospital databases (median = very robust) (rather easily available)
• Reduced prevalence rates in the elderly; more sensitive for young people at risk
• No adjustment necessary for BSA
• Rationale for cutoff of 1.5 (slightly above 1.33) is more funded than for the cutoff of 60 ml/min/1.73m²
• May serve as a simple and fast screening tool
• Only valid for IDMS-equivalent Scr