Acute renal failure
Definition and detection

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Definition

Acute Renal Failure

Acute Kidney Injury (AKI)
Definition

- Sudden decline in GFR and so
- Decrease in toxins excretion
- Maintain the volemic and ionic equilibrium

- Relatively few symptoms (except oliguria), so we need for the lab
At least now, we have a common definition for AKI
Section 2: AKI Definition

2.1.1: AKI is defined as any of the following (Not Graded):
- Increase in SCr by $\geq 0.3 \text{ mg/dl} (\geq 26.5 \mu\text{mol/l})$ within 48 hours; or
- Increase in SCr to $\geq 1.5$ times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume $< 0.5 \text{ ml/kg/h}$ for 6 hours.

2.1.2: AKI is staged for severity according to the following criteria (Table 2). (Not Graded)

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Staging of AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Serum creatinine</td>
</tr>
<tr>
<td>1</td>
<td>1.5–1.9 times baseline</td>
</tr>
<tr>
<td></td>
<td>OR $\geq 0.3 \text{ mg/dl} (\geq 26.5 \mu\text{mol/l})$ increase</td>
</tr>
<tr>
<td>2</td>
<td>2.0–2.9 times baseline</td>
</tr>
<tr>
<td>3</td>
<td>3.0 times baseline</td>
</tr>
<tr>
<td></td>
<td>OR Increase in serum creatinine to $\geq 4.0 \text{ mg/dl} (\geq 353.6 \mu\text{mol/l})$</td>
</tr>
<tr>
<td></td>
<td>OR Initiation of renal replacement therapy</td>
</tr>
<tr>
<td></td>
<td>OR, in patients $&lt; 18$ years, decrease in eGFR to $&lt; 35 \text{ ml/min per 1.73 m}^2$</td>
</tr>
</tbody>
</table>
AKI Diagnosis
(EPIDEMIOLOGY dimension)

• The goal is not to evaluate RENAL FUNCTION *per se*

• To capture AKI prognosis (mortality and RRT) through serum creatinine changes

• BACK CALCULATION OF BASELINE CREATININE (overestimation of AKI)
Criteria to define AKI

Diuresis and especially oliguria (<500ml/24h) remains specific

- Depend on perfusion and diuretics
- ARF with conserved diuresis
Oliguria as predictive biomarker of acute kidney injury in critically ill patients

John R Prowle¹, Yan-Lun Liu¹, Elisa Licari¹, Sean M Bagshaw², Moritoki Egi³, Michael Haase⁴, Anja Haase-Fielitz⁴, John A Kellum⁵, Dinna Cruz⁶, Claudio Ronco⁶, Kenji Tsutsui⁷, Shigehiko Uchino⁷ and Rinaldo Bellomo¹,³*

239 ICU patients

Oliguria vs. AKI according to Screat.

Incidence of AKI-Screat: 13.4%

6 hours of oliguria:
Sensitivity: 21%
Specificity: 93%
Positive predictive value: 9%
Negative predictive value: 97%

Figure 1 Receiver-operator characteristic analysis of the ability of varying durations of oliguria to predict RIFLE Injury (I) or more the next day. Receiver-operator characteristic (ROC) area under the curve = 0.75, 95% confidence interval (CI) 0.64-0.85.
Definition

• Creatinine

• New ARF biomarkers (cystatin C) and/or new AKI biomarkers (NGAL, KIM1, IL18....)
Serum creatinine: Analytical limitations

- Jaffe: Pseudochromogen: glucose, fructose, ascorbate, proteins, urate, acetoacetate, acetone, pyruvate => false « high »
- Bilirubins: false « low »
- Few (fewer) interferences with enzymatic methods
- Different Jaffe-Enzymatic methods, different calibration by different manufacturers
- IDMS-traceability (enzymatic methods)
Serum creatinine: Physiological limitations

- Production (relatively) constant but muscular production => serum creatinine is dependent of muscular mass, not only GFR
  - gender
  - age
  - ethnicity
  - Muscular mass(creatine)

- Tubular secretion of creatinine
  - 10 to 40%
  - Increase with decreased GFR
  - Unpredictable at the individual level

eGFR equations
CYSTATIN C

• cystéine protéase inhibitor (13 kDa)
• Produced by all nucleated cells (housekeeping gene)
• Freely filtrated through the glomerulus
• Fully reabsorbed and metabolized by the tubules
• Standardisation is possible (ERM-DA471/IFCC)
• Not influenced by muscular mass
Detection of decreased glomerular filtration rate in intensive care units: serum cystatin C versus serum creatinine

Pierre Delanaye 1*, Etienne Cavalier 2, Jérôme Morel 3, Manolie Mehdi 4, Nicolas Maillard 4, Guillaume Claisse 4, Bernard Lambermont 5, Bernard E Dubois 1, Pierre Damas 6, Jean-Marie Krzesinski 1, Alexandre Lautrette 7 and Christophe Mariat 4

47 patients
hemodynamically stable
Avec Scr <1,5 mg/dL
GFR measured by iohexol urinary clearance
SERUM CREATININE
R=0.5

CYSTATIN
R=0.7

Figure 1: Correlations between the inverse of creatinine and GFR (upper) \( y = 0.09024 + 0.0009156x \) and the inverse of cystatin C and GFR (lower) \( y = 0.4939 + 0.004871x \).

Figure 2: ROC curves analysis for cystatin C (—) (AUC = 0.942) and creatinine (-----) (AUC = 0.799) to detect GFR under 60 mL/min (p = 0.014).

Delanaye et al. BMC Nephrology 2014, 15:9
DETECTION OF AKI

Herget-Rosenthal et al., Kidney Int 2004  85 adultes, general ICU, S-creatinine rise > 50%
Cystatin C

• Potentially of interest
• Relatively few studies
• There are also non-GFR determinants of cystatin C
• More expensive
• Cost-effectiveness not definitively proven
What about eGFR equations?

• They are valid at the equilibrium
Statistics

• Good correlation: a “sine qua non” condition but insufficient
• Bias: mean difference between two values = the systematic error
• Precision: SD around the bias = the random error
• Accuracy 30% = % of eGFR between ± 30% of measured GFR
Detection of decreased glomerular filtration rate in intensive care units: serum cystatin C versus serum creatinine

Pierre Delanaye¹*, Etienne Cavalier², Jérôme Morel³, Manolie Mehdi⁴, Nicolas Maillard⁴, Guillaume Claisse⁴, Bernard Lambermont⁵, Bernard E Dubois¹, Pierre Damas⁶, Jean-Marie Krzesinski¹, Alexandre Lautrette⁷ and Christophe Mariat⁴

Table 3 Predictive performances of the MDRD, CKD-EPI SCR, CKD-EPI SCysC, and combined equations in ICU patients

<table>
<thead>
<tr>
<th>GFR estimates</th>
<th>Bias (mL/min)</th>
<th>Absolute Precision mL/min</th>
<th>Accuracy 30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDRD</td>
<td>+35</td>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>+1</td>
<td>37</td>
<td>60*</td>
</tr>
<tr>
<td>CKD-EPI Scyst</td>
<td>-26</td>
<td>36</td>
<td>53</td>
</tr>
<tr>
<td>CKD-EPI combined</td>
<td>-12</td>
<td>35</td>
<td>62</td>
</tr>
</tbody>
</table>

*: p < 0.05 versus MDRD study equation.
Retooling the Creatinine Clearance Equation to Estimate Kinetic GFR when the Plasma Creatinine Is Changing Acutely

Sheldon Chen

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- Kinetic eGFR: to analyze kidney function in the acute setting
- Initial creatinine content, Vd, creatinine production rate and the quantitative difference between consecutive Scr over a short period of time
Kinetic GFR

\[ KeGFR = \frac{SSP_{Cr} \times CrCl}{MeanP_{Cr}} \times \left(1 - \frac{24 \times \Delta P_{Cr}}{\Delta Time(h) \times Max\Delta P_{Cr}/Day}\right) \]

SSPCr= baseline creatinine (the lowest known for the patient)  
CrCl= MDRD or CKD-EPI  
Mean PCr= mean of considered creatinine  
\(\Delta P_{Cr}\)= changes in creatinine  
\(\Delta time\)= interval in hours between two creatinine  
\(\Delta MaxP_{cr}\)= the maximal change (increase) in the plasma creatinine that can occur per day if renal function is completely lost ~ 1.7 mg/dL
Kinetic Estimation of GFR Improves Prediction of Dialysis and Recovery after Kidney Transplantation

Timothy J. Pianta1,2*, Zoltan H. Endre1,2, John W. Pickering3, Nicholas A. Buckley3, Philip W. Peake1

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Kinetic eGFR and Novel AKI Biomarkers to Predict Renal Recovery

Antoine Dewitte,*† Olivier Joannès-Boyau,* Carole Sidobre,* Catherine Fleureau,* Marie-Lise Bats,† Philippe Derache,† Sebastien Leuillet,§ Jean Ripoche,+ Christian Combe,‡§ and Alexandre Ouattara*†

Conclusions

• Monitoring diuresis and serum creatinine
• Cystatin C: maybe of interest
• eGFR equations lack of precision
• Kinetic eGFR: simple, based on creatinine, but need to be validated in future studies
• Now we are moving from acute renal failure detection/monitoring to acute kidney injury