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 olguria), so we need for the lab

Definition, classification

- **At least now, we have a common definition for AKI**

KDIGO Clinical Practice Guideline for Acute Kidney Injury

VOLUME 2 | ISSUE 1 | MARCH 2012

http://www.kidney-international.org

Section 2: AKI Definition

2.1.1: AKI is defined as any of the following (*Not Graded*):

- **Increase in SCr by ⩾0.3 mg/dl (⩾26.5 μmol/l) within 48 hours; or**
- **Increase in SCr to ⩾1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or**
- **Urine volume <0.5 ml/kg/h for 6 hours.**

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

Table 2 | Staging of AKI

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ⩾0.3 mg/dl (⩾26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ⩾12 hours
3	3.0 times baseline OR Increase in serum creatinine to ⩾4.0 mg/dl (⩾353.6 μmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ⩾24 hours OR Anuria for ⩾12 hours

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)

Definition

Criteria to define AKI

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

-Depend on perfusion and diuretics

-ARF with conserved diuresis

RESEARCH Open Access

Oliguria as predictive biomarker of acute kidney injury in critically ill patients

John R Prowle[1], Yan-Lun Liu[1], Elisa Licari[1], Sean M Bagshaw[2], Moritoki Egi[3], Michael Haase[4], Anja Haase-Fielitz[4], John A Kellum[5], Dinna Cruz[6], Claudio Ronco[6], Kenji Tsutsui[7], Shigehiko Uchino[7] and Rinaldo Bellomo[1,8*]

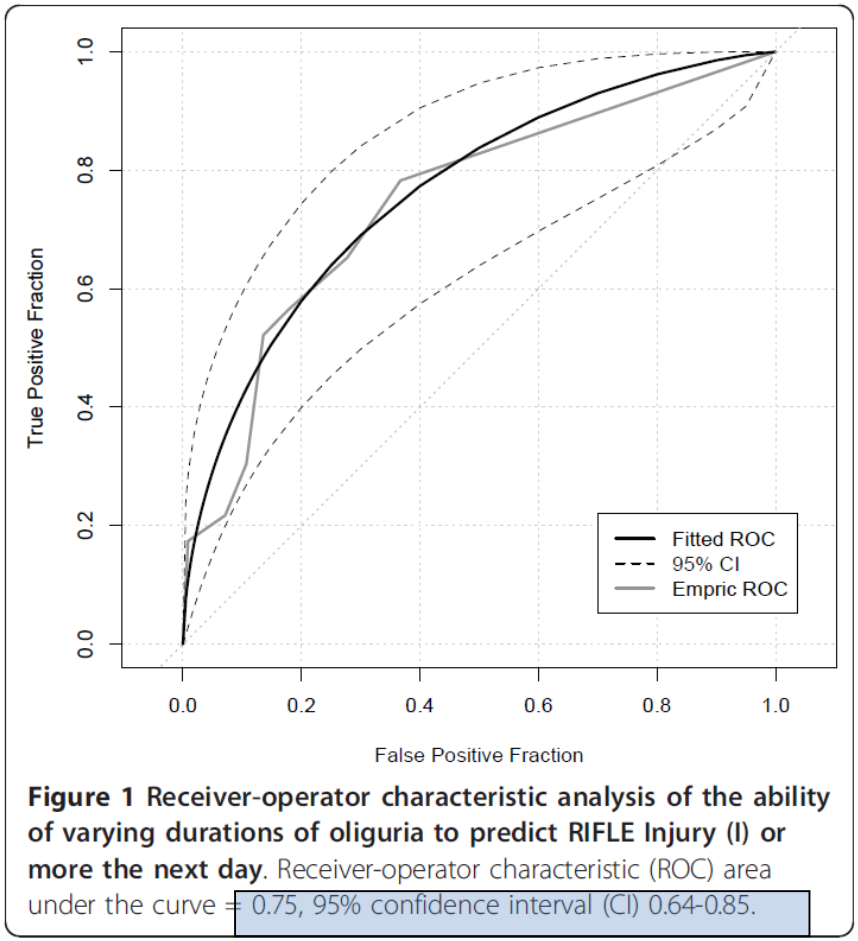


Figure 1 Receiver-operator characteristic analysis of the ability of varying durations of oliguria to predict RIFLE Injury (I) or more the next day. Receiver-operator characteristic (ROC) area under the curve = 0.75, 95% confidence interval (CI) 0.64-0.85.

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%

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 muscualr 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

Perrone RD, Clin Chem, 1992, p1933

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

Delanaye *et al. BMC Nephrology* 2014, **15**:9
http://www.biomedcentral.com/1471-2369/15/9

BMC Nephrology

RESEARCH ARTICLE Open Access

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
hemodynamiccaly stable
Avec Scr <1,5 mg/dL
GFR measured by iohexol urinary clearance

SERUM CREATININE R=0.5

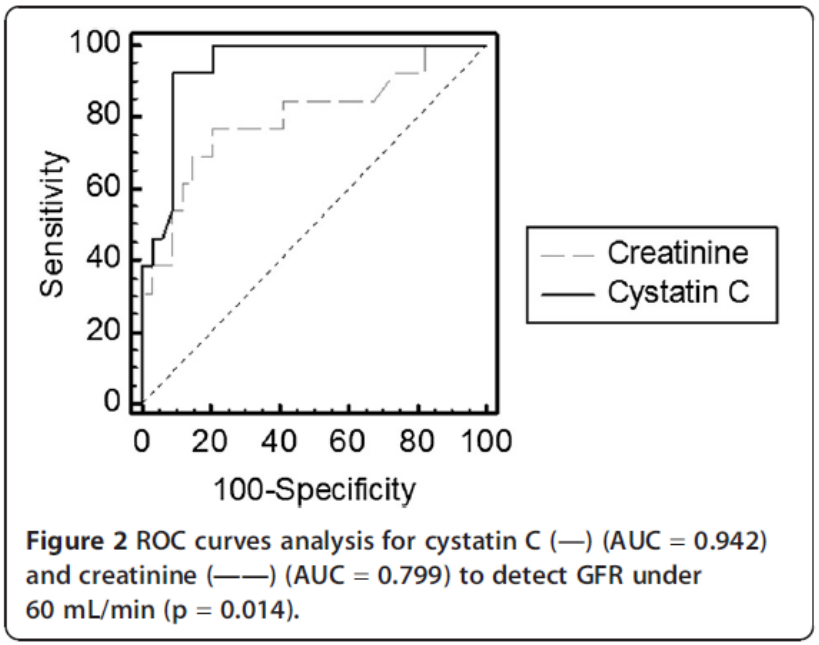


Figure 2 ROC curves analysis for cystatin C (—) (AUC = 0.942) and creatinine (——) (AUC = 0.799) to detect GFR under 60 mL/min (p = 0.014).

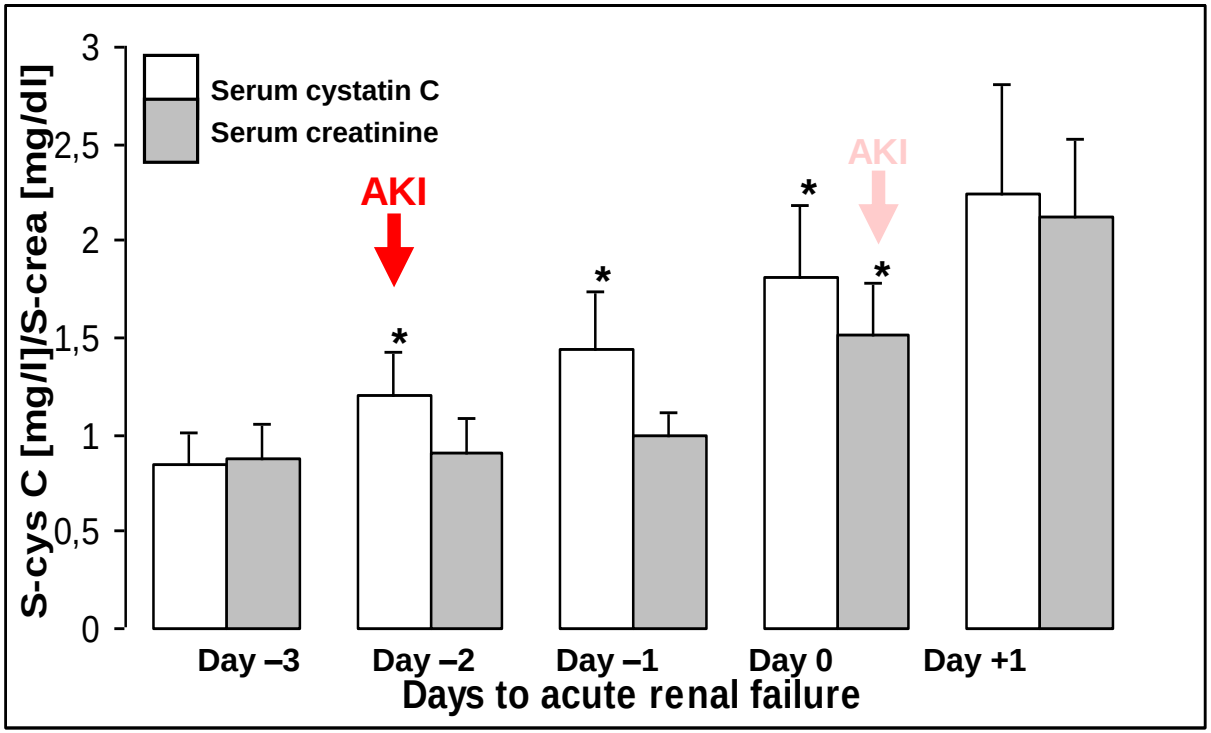
CYSTATIN =0.7

GFR (iohexol) (mL/min)

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).

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

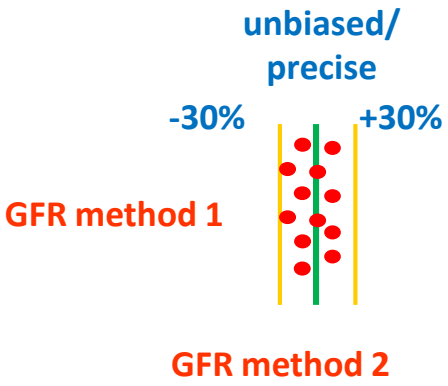
- Potentially of interest
- Relatively few studies
- There are also non-GFR determinants of cystatin C
- More expensive
- Cost-effectiveness not definitively proven

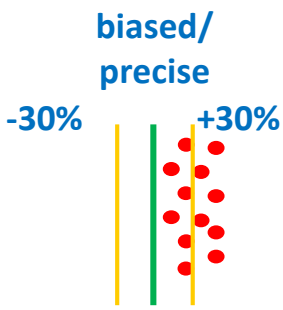
What about eGFR equations?

- 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





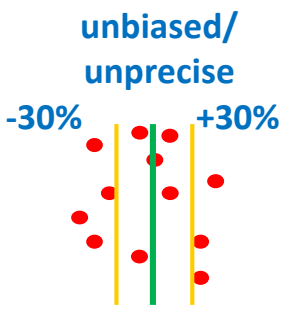


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Table 3 Predictive performances of the MDRD, CKD-EPI SCr, CKD-EPI SCysC, and combined equations in ICU patients

GFR estimates	Bias (mL/min)	Absolute Precision mL/min	Accuracy 30%
MDRD	+35	70	40
CKD-EPI	+ 1	37	60*
CKD-EPI Scyst	−26	36	53
CKD-EPI combined	−12	35	62

**: $p < 0.05$ versus MDRD study equation.*

SPECIAL ARTICLE www.jasn.org

Retooling the Creatinine Clearance Equation to Estimate Kinetic GFR when the Plasma Creatinine Is Changing Acutely

Sheldon Chen

Division of Nephrology and Hypertension, Department of Medicine, Northwestern Feinberg School of Medicine, Chicago, Illinois

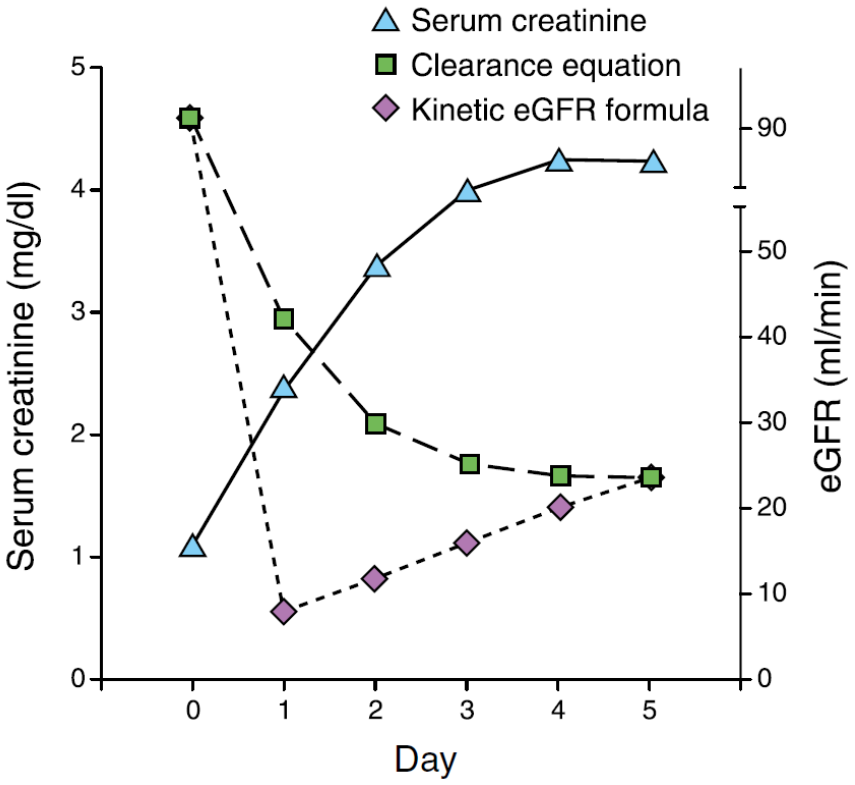
J Am Soc Nephrol 24: 877–888, 2013.

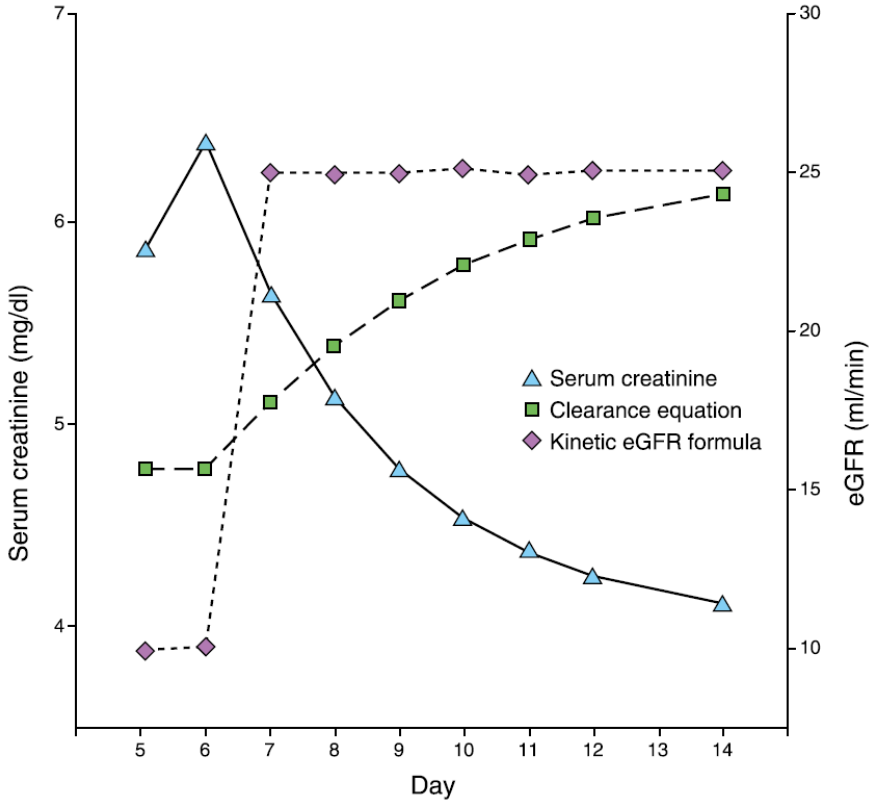
- Kinetic eGFR: to analyze kidney function in the acute setting
- Initial creatinine content, Vd, creatinine production rate and the quantitative difference between consecutive Scr over a short period of time

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
ΔPCr= changes in creatinine
Δtime=interval in hours between two creatinine
ΔMaxPcr=the maximal change (increase) in the plasma creatinine that can occur per day if renal function is completely lost ~ 1,7 mg/dL


Serum creatinine
Clearance equation
Kinetic eGFR formula
Serum creatinine (mg/dl)
eGFR (ml/min)
Day
0
1
2
3
4
5
10
20
30
40
50
90


Serum creatinine
Clearance equation
Kinetic eGFR formula
Serum creatinine (mg/dl)
eGFR (ml/min)
Day
4
5
6
7
8
9
10
11
12
13
14
15
20
25
30

PLOS | ONE

RESEARCH ARTICLE

Kinetic Estimation of GFR Improves Prediction of Dialysis and Recovery after Kidney Transplantation

Timothy J. Pianta[1,2]*, Zoltan H. Endre[1,3], John W. Pickering[3], Nicholas A. Buckley[4], Philip W. Peake[1]

1 Prince of Wales Clinical School, University of New South Wales, Sydney, Australia, **2** Melbourne Medical School, University of Melbourne, Melbourne, Australia, **3** Department of Medicine, University of Otago, Christchurch, New Zealand, **4** Clinical Pharmacology, University of Sydney, Sydney, Australia

* timothy.pianta@nh.org.au

PLOS ONE | DOI:10.1371/journal.pone.0125669 May 4, 2015

Kinetic eGFR and Novel AKI Biomarkers to Predict Renal Recovery

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

Clin J Am Soc Nephrol 10: 1900–1910, 2015.

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