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A spurious decline in kidney function

A reality check

Deepak L Vardesh, Jeremy Elton Frazier, Ken-Soon Tan

CASE

A man aged 70 years was referred to a renal clinic by his general practitioner for evaluation of a decline in his renal function. He had a history of hypertension, for which he was taking perindopril and amlodipine in combination, and left nephrectomy for renal cell carcinoma in 2013.

A drop in his estimated glomerular filtration rate (eGFR) from a baseline of approximately 70 mL/min in February 2019 to 51 mL/min in May 2019 was noted with no obvious cause. His perindopril was withheld in view of this decline. However, by the time he was reviewed in the clinic, his renal function had recovered and he had recommenced perindopril.

On perusing his blood tests, it was noted that he had significantly different eGFR reported for the same serum creatinine value (eGFR of 51 mL/min and 68 mL/min for a

serum creatinine value of 98 $\mu\text{mol/L}$). Between May and August 2019, when a lower eGFR was reported, the serum creatinine reference range for females (45–85 $\mu\text{mol/L}$) had been used instead of that for males (60–115 $\mu\text{mol/L}$). The patient's results are shown in Table 1.

The patient had a unisex first name, likely resulting in an inadvertent biological sex misassignment and a spuriously low eGFR. This was subsequently corrected, resulting in an improvement in his eGFR.

On contacting the reporting laboratory, it was established that the correct biological sex had been ascribed to the patient on the request form, but the error had occurred at the level of the laboratory, likely from an error of manual transcription.

QUESTION 1

What is the most commonly employed marker of renal function?

QUESTION 2

What factors affect serum creatinine levels?

QUESTION 3

How is renal function reported in the laboratory?

QUESTION 4

What are some circumstances in which the use of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to calculate eGFR is unreliable?

ANSWER 1

Serum creatinine is the most commonly employed endogenous marker of renal function. It is produced from muscle and excreted in the urine, primarily through glomerular filtration. A proportion of serum creatinine is secreted by the proximal tubule, and this increases significantly with advanced renal impairment. Hence, measurement of creatinine clearance can overestimate GFR.¹

ANSWER 2

Serum levels depend on various factors including muscle mass, sex, age and diet. Certain medications, such as trimethoprim and cimetidine, can

Table 1. The patient's serum creatinine and estimated glomerular filtration rate (eGFR) between May 2018 and November 2019

	May 2018	February 2019	May 2019	July 2019	August 2019	September 2019	October 2019	November 2019
Serum creatinine ($\mu\text{mol/L}$)	96	94	98	99	97	98	101	95
eGFR (mL/min)	70	71	51	50	52	68	65	70

Box 1. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation

Glomerular filtrate rate = $141 \times \text{minimum (serum creatinine}/k, 1)^{\alpha} \times \text{maximum (serum creatinine}/k, 1)^{-1.209} \times 0.993^{0.9e} \times 1.018$ (if female) $\times 1.159$ (if black)

k is 0.7 for females and 0.9 for males

α is -0.329 for females and -0.411 for males

Minimum indicates the minimum of serum creatinine/ k or 1

Maximum indicates the maximum of serum creatinine/ k or 1

interfere with tubular secretion of creatinine and increase serum levels.¹

ANSWER 3

In Australia, renal function is currently reported as eGFR using the creatinine-based CKD-EPI equation. This is outlined in Box 1.²

ANSWER 4

The equation has not been validated in pregnancy. It is unreliable in patients with extremes of muscle mass and those with rapidly fluctuating renal function.^{2,3}

Key points

- It is important to look not only at the eGFR but also at the reported serum creatinine value and the reference range simultaneously.
- Serum creatinine is the most commonly used endogenous marker of kidney function and is affected by several factors including biological sex.
- Care should be taken to enter demographic details accurately on the request form.
- The creatinine-based CKD-EPI equation is currently used to estimate glomerular filtration rate.
- If in doubt, the eGFR should be calculated using one of the readily available online calculators (eg <https://kidney.org.au/health-professionals/egfr-calculator>).

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