Calculating glomerular filtration rate in a young man with a large muscle mass

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Clinical record

A 29-year-old man presented with a history of increasing lethargy and malaise for 3 months. He had lost 3 kg in weight and noticed mild ankle oedema. His previous medical history was unremarkable, and he had no relevant family history. He had been a professional body builder for 10 years, previously competing at high levels. He attended a gymnasium daily for weight-lifting. His dietary protein intake was very high (3.5 g/kg daily) and he took 5 g/day creatine powder supplement. Although he was not taking any regular medication, he admitted to extensive use of anabolic steroids (including testosterone and nandrolone) over a 10-year period.

On examination, he weighed 103 kg and was 175 cm tall (body surface area, 2.24 m^2) and his blood pressure was 195/110 mmHg. His chest was clear, and cardiovascular examination showed no abnormalities except for mild peripheral oedema. Investigations revealed a serum creatinine level of 1346 μmol/L (reference range [RR], 30–120 μmol/L) and a urea level of 63.5 mmol/L (RR, 2.5–7.5 mmol/L). Values obtained in other investigations included: haemoglobin, 112 g/L (RR, 125–175 g/L); albumin, 35 g/L (RR, 34–50 g/L); potassium, 3.8 mmol/L (RR, 3.5–5.0 mmol/L); corrected calcium 1.98 mmol/L (RR, 2.10–2.55 mmol/L); phosphate, 2.95 mmol/L (RR, 0.81–1.45 mmol/L); and parathyroid hormone, 31.8 pmol/L (RR, 1.3–6.8 pmol/L). Results of a mid-stream urine test were unremarkable except for protein 3+, and a 24-hour urine collection revealed 10.7 g/day proteinuria. An ultrasound examination of the renal tract showed two normal-sized kidneys without hydronephrosis, but with diffusely increased parenchymal echogenicity.

A renal biopsy confirmed a diagnosis of focal segmental glomerulosclerosis, with marked tubulointerstitial damage. Counselling was provided, with information about dialysis and kidney transplantation options. The patient was prescribed amlodipine, which gave good blood pressure control, and calcium carbonate as a phosphate binder. He was also given dietary advice. As he had only mild symptoms, and to avoid using a tunnelled dialysis catheter, haemodialysis was not immediately initiated.

Calculations of overall renal function gave varying results (Box 1). Calculated from the serum creatinine level at presentation, the estimated glomerular filtration rate (eGFR) (based on the abbreviated MDRD [modification of diet in renal disease]) was 5.18 mL/min/1.73 m^2. The full MDRD equation (6-variable) gave a GFR of 4.96 mL/min/1.73 m^2. However, the Cockcroft–Gault formula, weight included, gave a GFR of 8.05 mL/min/1.73 m^2, and 24-hour urine collection gave results for creatinine clearance of 12.97 mL/min/1.73 m^2. A radioisotope nuclear renal scan (DTPA [diethylenetriaminepentaacetate]) to better clarify the degree of renal impairment showed equal function of both kidneys and a GFR of 13.51 mL/min/1.73 m^2.

Over the following few weeks, with changes in diet and cessation of creatine supplements, serum creatinine and urea levels decreased slightly, and arrangements for an early living-related renal transplant were formulated. However, because of worsening uraemic symptoms, dialysis was eventually commenced and was required for 3 months before successful transplantation with a kidney donated by the patient's mother. ◆

Serum creatinine level, the most commonly used measure of kidney function in clinical practice, varies with factors other than kidney function. These include age, sex, muscle mass, and dietary protein intake. Glomerular filtration rate (GFR) is therefore widely accepted as a better marker. Numerous equations using the serum creatinine level have been developed to calculate estimated GFR (eGFR) (Box 2). Recently, automated reporting of eGFR using the MDRD (modification of diet in renal disease) formula has been introduced, but limitations exist, especially with extremes of body size. Our patient illustrates the difficulties of calculating GFR for a person with a large muscle mass, with different methods giving widely varying results.

The recently published CARI (Caring for Australasians with renal impairment) guidelines recommend that serum creatinine level alone should not be used to measure kidney function, because of the multitude of factors other than renal function that can affect this marker.[1,2] Serum creatinine is derived from the metabolism of creatine in muscle and the generation of creatinine tends to be proportional to muscle mass.

In adults, the abbreviated (4-variable) MDRD, the 6-variable MDRD, and the Cockcroft–Gault equations generally provide reliable eGFRs. The Cockcroft–Gault formula is probably the most widely recognised formula for conversion of serum creatinine level, although with reductions below 60 mL/min it becomes increasingly inaccurate compared with the MDRD formula.

Recently, the abbreviated MDRD formula has been used in the automated laboratory reporting of eGFR in Australia, given extensive validation with no correction needed for body surface area. It is important to note that the different units for GFR measurements

1 Variations in estimated and measured glomerular filtration rate (GFR) for the same patient (serum creatinine level, 1346 μmol/L; body surface area, 2.24 m^2)

Method of calculation	GFR (mL/min)	GFR (mL/min/1.73 m^2)
MDRD	6.42	4.96
MDRD (abbreviated)	6.71	5.18
Reciprocal serum creatinine	7.33	5.66
Cockcroft–Gault	10.43	8.05
Creatinine clearance (24-h urine)	16.80	12.97
Radioisotope scan (DTPA)	17.50	13.51

MDRD = Modification of diet in renal disease.
DTPA = diethylenetriaminepentaacetate. ◆

2 Equations for calculating estimated glomerular filtration rate (eGFR)

Body surface area (BSA): $BSA\ (m^2) = 0.007184 \times (\text{height [cm]})^{0.725} \times (\text{weight [kg]})^{0.425}$

Cockcroft–Gault formula: $GFR\ (mL/min) = (140 - age) \times weight \times 1.228/SCr \times (0.85, \text{if female})$

Reciprocal serum creatinine: $GFR\ (mL/min) = 100/SCr \times 100$

MDRD (6-variable): $GFR\ (mL/min/1.73\,m^2) = 170 \times (SCr/88.4)^{-0.999} \times age^{-0.176} \times (SU \times 2.78)^{-0.17} \times albumin^{0.318} \times (0.762, \text{if female}) \times (1.18, \text{if African American})$

Abbreviated MDRD (4-variable): $GFR\ (mL/min/1.73\,m^2) = 186 \times (SCr/88.4)^{-1.154} \times age^{-0.203} \times (0.742, \text{if female}) \times (1.210, \text{if African American})$

GFR = glomerular filtration rate. SCr = serum creatinine level (μmol/L). SU = serum urea level (mmol/L). MDRD = Modification of diet in renal disease. ◆

(mL/min for Cockcroft–Gault versus mL/min/1.73 m^2 for MDRD) can create some discrepancy in their comparison (see Box 1).

MDRD and Cockcroft–Gault equations are essentially rescaled serum creatinine levels with the same pitfalls as using the serum creatinine level itself. They are based on statistical models predicting averages, and our patient was not average. Therefore, clinical judgement is always required with eGFR, and the clinician has the advantage of being able to consider dietary history and physical examination — factors not considered in these equations.

Previously, 24-hour urine collections to assess creatinine clearance were commonly used. These are inconvenient, inaccurate because of inadequate collection techniques, and, with severe renal impairment, creatinine clearance overestimates GFR. With worsening impairment there is an increase in tubular creatinine secretion, ranging from 10% to 50%, and therefore variations may alter the relationship between serum creatinine level and GFR.[3]

Nuclear medicine scans provide validated direct measures of GFR and are useful in circumstances of extremes of body size or age, high or low dietary intake of creatinine or creatine supplements, and patients with muscle disease or atrophy. They determine renal clearance of exogenous filtration markers, most commonly DTPA (diethylenetriaminepentaacetate), and provide acceptably accurate measurements, although it is recognised that they may overestimate GFR.[1,2] The disadvantages of radionucleotide GFR measurement relate to safety with the use of radiolabelled compounds and the cost.

In our patient, different methods of GFR measurement provided a range from 4.96 to 13.51 mL/min/1.73 m^2, depending on the equation or the investigation used. The CARI guidelines suggest that dialysis should be commenced when GFR falls below 10 mL/min/1.73 m^2, if associated with symptomatic uraemia or malnutrition, or below 6 mL/min/1.73 m^2, if asymptomatic.[4] Initiation of dialysis in our patient, with risks of temporary dialysis access, was weighed against the decision to wait for a renal transplant, given that the patient was initially relatively asymptomatic. The best option for renal replacement therapy is kidney transplantation where appropriate, and the patient's mother had volunteered as a potential donor. The commencement of dialysis is sometimes a difficult decision and clinicians need to recognise the inaccuracies with eGFR measurement. Symptoms, treatment options and rate of GFR decline are among a multitude of factors that must be taken into account in the decision to initiate dialysis.

Having illustrated some of the limitations in determining renal function using eGFR, we strongly advocate routine automated reporting in clinical practice. eGFR is extremely useful for identifying patients at risk of progressive chronic kidney disease and correlates well with complications, including an increased risk of cardiovascular morbidity and mortality. An educational program is underway, involving distributed written material and short courses organised by Kidney Health Australia, to ensure that information is available to help health professionals interpret eGFR values. It should be appreciated that there are specific clinical settings in which eGFR is not appropriate and GFR should be measured directly through other methods.

Lessons from practice

- Estimated glomerular filtration rate (eGFR) may be inaccurate in patients whose body size and muscle mass, or dietary intake (eg, high protein diets and creatine supplements), are at the extremes of the normal range.
- In such patients, formal measurement of GFR by radioisotope nuclear renal scan should be undertaken.
- eGFR should not be relied on as the sole determinant in making decisions about the commencement of dialysis; investigations should be interpreted in conjunction with the overall clinical picture. ◆

Competing interests

None identified.

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