Laboratory tests of renal function

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Abstract

The kidneys are vital organs in the management of fluid balance, waste product removal, electrolyte homeostasis, acid–base balance and endocrine function. Waste products removed by the kidney include urea, uric acid, creatinine and other foreign products with similar physiochemical properties. Urea and uric acid are by products of protein metabolism and creatinine is generated by the metabolism of creatine compounds from muscle. The kidney regulates fluid and electrolyte balance through controlling the composition and volume of urine. In the proximal convoluted tubule and the loop of Henle, 90% of sodium, potassium, calcium and magnesium are reabsorbed. Acid–base balance is achieved by regulating the excretion of hydrogen ions and bicarbonate buffering. The kidney also has a number of endocrine functions including the production of renin and erythropoietin as well as hydroxylation of vitamin D. The kidneys receive 25% of cardiac output, generating 170–200 litres of ultrafiltrate per day. Urine output is approximately 1.5 litres per day, which is concentrated ultrafiltrate through selective reabsorption of solutes and water. In this article we will discuss tests frequently used to assess renal function.

Keywords Acute kidney injury; biomarkers; creatinine; creatinine clearance; glomerular filtration rate; renal function; urea; urinalysis

Royal College of Anaesthetists CPD Matrix: 1A01, 1A03, 2A03

Learning objectives

After reading this article, you should be able to:
- list six laboratory tests that assess renal function
- calculate glomerular filtration rate
- state normal blood and urine biochemistry values

Assessment of renal function

Assessment of renal function is performed through history and examination in conjunction with the tests listed in Table 1 to ensure a complete clinical picture is formed. The findings may help to diagnose a renal or systemic disorder.

Glomerular filtration rate (GFR)

GFR is the rate that plasma is cleared of substances by filtration of blood through the glomerulus into the Bowman's capsule. Measuring the clearance of specific substances is a surrogate of GFR, which in turn provides an overall index of renal function. Renal clearance is the volume of plasma cleared of an ideal substance per unit time, measured in ml/min. The ideal particle measured should be freely filtered and not reabsorbed, secreted or metabolized along the path of the nephron, otherwise this will lead to an inaccurate calculation of GFR.

The equation used for the calculation of GFR is:

$$Cs = (Us \times V)/Ps$$

where Cs is the volume of plasma cleared of the substance per minute, Us is the urinary concentration of the substance, V is the volume of urine produced per minute and Ps is the plasma concentration of the substance.

A number of exogenous substances have been used to calculate GFR. Such as ^{51}creatinine EDTA, inulin, ^{124} iothalamate and cystatin C.[1] Radioisotopes are not commonly used in clinical practice, as there are issues related to the safe disposal of the isotope and the prolonged clearance from patients with chronic renal disease. Cystatin C is freely cleared at the glomerulus; however, its serum concentration is influenced by many other factors such as malignancy and glucocorticoids making it less reliable than creatinine.[1]

Creatinine clearance

Given the practical issues discussed above, creatinine is the most commonly used endogenous marker for assessing renal function.

Formed from the breakdown of creatine and phosphocreatine from skeletal muscle, the metabolism occurs at a relatively constant rate. Creatinine is freely filtered at the glomerulus and not reabsorbed; however, it is actively secreted by the proximal convoluted tubule, which can be up to 15%. This may lead to over estimation in creatinine clearance. However, there is some attenuation by the plasma concentration also being overestimated. Secretion at the proximal convoluted tubule can be abolished by cimetidine to get a true reading of GFR.[2]

Creatinine clearance is calculated from a 24-hour urinary collection and serum creatinine sample taken during the time of collection. Serum creatinine concentration is assumed to be stable during the 24 hour period. Creatinine clearance has also been performed over shorter periods in catheterized patients.

Problems related to performing and measuring creatinine clearance include time taken, inconvenience to the patient, errors in urine collection and extrarenal degradation of creatinine.

Creatinine-based equations of GFR

A number of formulae have been developed to calculate creatinine clearance. However, all have limitations as they do not take into account the variables that affect serum creatinine levels. These factors include age, height, weight, gender, race, exercise and diet.

The two most commonly used formulae are Cockcroft-Gault equation (CG) and Modification of Diet in Renal Disease study group (MDRD).

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Commonly used tests of renal function

Urea	Full blood count
Creatinine	Na^+
Creatinine clearance	K^+
Urine microscopy	Ca^{2+} and PO_4^-
Urine osmolarity	Parathyroid hormone

Table 1

The CG model estimates creatinine clearance (eC_{cr}), and hence GFR, based on serum creatinine, age, sex and body mass. The original formula used weight in kilogrammes and creatinine in milligrams per decilitre, as is standard in the USA:

eC_{cr} = ((140 − age) × weight (kg) × (0.85 if female))/72 × serum creatinine (mg/dl)

Serum creatinine in the UK is measured in micromoles per litre, the formula is modified and a constant is used for both men and women to complete the estimation:

eC_{cr} =((140 − age) × weight(kg) × constant (m/f))/serum creatinine (μmol/litre)

The constant is 1.23 for men and 1.04 for women. This formula is well supported as it provides a simple way to estimate GFR. It overestimates GFR in obese or oedematous individuals and does not account for ethnicity.

The MDRD Study Group developed an alternative to this formula, indexed to body surface area. In its original form, it used six measurements to estimate GFR (eGFR), including blood urea nitrogen (BUN) and albumin levels. A basic four-variable form of the calculation containing serum creatinine, race, age and gender is:

eGFR (ml/minute/1.73 m^2) = 186 × (serum creatinine (μmol/litre)/88.4)$^{-1.154}$ × age$^{\mathbf{-0.203}}$ × 1.12 (if black) × 0.742 (if female)

However, the MDRD estimate is a poor measure of GFR in healthy individuals without renal pathology.[3] For initial diagnosis of chronic kidney disease the CKD-EPI formula is recommended by NICE as the most appropriate method to estimate GFR; it is based on the four-variable form of the MDRD equation but is more accurate, especially at higher GFR.[4] These equations are not validated in children, in whom an alternative, the Schwartz equation (Table 2), should be used. Height in centimetres is multiplied by an age-dependent constant; this total is then divided by the serum creatinine concentration to give an estimation of GFR indexed to body surface area. Creatinine-based equations have many limitations, reflecting the variability of creatinine production with many factors. Diuretics, spironolactone and triamterene, as well as trimethoprim, cimetidine

Equations for assessment of renal function

1 The Cockroft-Gault equation (UK)

$$eC_{cr} = \frac{(140-\text{age})\times\text{weight (kg)}\times(\text{constant})}{\text{Serum creatinine (mol/litre).}}$$

eC_{cr} = estimated creatine clearance

The constant is 1.23 for men and 1.04 for women.

This formula provides a simple way to estimate GFR.

2 The Modification of Diet in Renal Disease Study Group equation

eGFR (ml/minute/1.73 m^2) = 186 × (serum creatinine (μmol/l)/88.4)$^{-1.154}$ × age$^{\mathbf{-0.203}}$ × 1.12 (if black) × 0.742 (if female)

3 CKD EPI equation (for estimating GFR expressed for specified race, sex and serum creatinine in mg/dl)

$$GFR = 141 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018 \text{ (if female)} \times 1.159 \text{ (if black)}$$

where:

S_{cr} is serum creatinine in mg/dl,

κ is 0.7 for females and 0.9 for males,

α is −0.329 for females and −0.411 for males,

min indicates the minimum of S_{cr}/κ or 1, and

max indicates the maximum of S_{cr}/κ or 1.

4 The Schwartz equation

$$eC_{cr}\ (\text{ml/minute/1.73 m}^2) = \frac{\text{length in cm}\times k}{\text{serum creatinine(mg/dl)}}$$

k = 0.33 for prem infants

k =0.45 for infants term to 1 year

k = 0.55 for children 1 year to 13 years

k = 0.70 in adolescent males (females constant remains at 0.55)

5 Free Water Clearance (FWC)

$FWC = V (1 - U_{osm}/P_{osm})$

V = urine volume

U_{osm} = urine osmolality

P_{osm} = plasma osmolality

Chadwick L et al. 2015 Anaesthesia and Intensive care.

Table 2

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