Diagnosing Chronic Kidney Disease

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Chronic kidney disease (CKD) is defined as either evidence of kidney damage or reduction in glomerular filtration rate (GFR) of < 60 ml/min/1.73m^2 persistent for three or more months. This definition was developed by the Kidney Disease Outcomes Quality Initiative (K/DOQI) and has been internationally accepted. Kidney damage has been defined as pathologic abnormalities or markers of kidney damage (such as proteinuria) including abnormalities in blood or urine tests or imaging studies. CKD has been divided into five stages (Table 1).[1]

Table 1
Five stages of CKD

Stage	GFR	Description
1	≥ 90	Kidney damage with normal or ↑ GFR
2	60-89	Kidney damage with mildly ↓ GFR
3	30-59	Moderate ↓ GFR
4	15-29	Severely ↓ GFR
5	< 15	Kidney failure

CKD: Chronic kidney disease
GFR: Glomerular filtration rate

Using this definition of CKD, the prevalence of CKD is very common affecting about 11% of the adult population in the US.

For the busy primary care physician, remembering the cut of GFR value of 60 ml/min/1.73m^2 and 30 ml/min/1.73m^2 should be sufficient. If GFR is > 60 ml/min/1.73m^2 then diagnosis of CKD requires evidence of kidney damage and if GFR is persistently < 30 ml/min/1.73m^2 then there is severe decrease in GFR and referral to a nephrologist should be considered. Using this definition of CKD, the prevalence of CKD is very common affecting about 11% of the adult population in the US.[2] Extrapolating from this data, about 1.5 million Canadian adults are affected by CKD.[3] A minority of this population will progress to end stage renal disease requiring renal replacement therapy with its attendant loss of quality of life and high cost of treatment, but the major risk to patients with CKD is CV mortality and morbidity.[4] Thus, it is imperative to identify these patients early so that interventions that improve CV mortality and morbidity and delay progression of CKD can be implemented in a timely manner.

Traditionally, serum creatinine was relied upon to measure kidney function which resulted in under diagnosis of CKD especially in the elderly and in women.[5] Detection of CKD remained poor even among patients whose kidney function was tested.[5] Recently, much research has been done in improving detection of CKD. Kidney function is defined as the GFR which is the amount of plasma filtered through the glomerulus per unit of time. Mathematical formulae which estimate GFR such as Cockcroft-Gault[6] and the Modification of Diet in Renal Disease (MDRD)[7] reliably predict GFR and have been shown to markedly improve detection of CKD. Akbari, *et al* using the Cockcroft-Gault formula improved detection of CKD by 400% in a family practice clinic in Ottawa by reporting the estimated GFR (eGFR) and educating physicians about this new test.[8] Not only was there improvement in detection of CKD but also the gender bias of creatinine was abolished with reporting of eGFR.[8] The Cockcroft-Gault formula requires weight in its calculation where as the MDRD formula assumes a body surface area of 1.73m^2 and does not require weight in its calculations. For the laboratories, it is much easier to report the eGFR derived from the MDRD as it only requires age, gender, serum creatinine and race in its calculation. All of the variables except race are available to the labs to easily do the calculation. The laboratories report the value for Caucasians and under the results will indicate that if your patient is African, multiply the results by 1.212. There are several limitations to the MDRD formula (Table 2) which a clinician needs to take into account when interpreting the results of eGFR by MDRD formulae. Because of the variation in measurement of serum creatinine by different laboratories, efforts are underway to standardize the measurement of serum creatinine and thus eGFR.[9]

Table 2

Limitations to the MDRD formula

- Not reliable for eGFR > 60 ml/min/1.73m^2 (formula does not work well)
- Not reliable for extremes of weight or abnormal body composition such as amputees, paraplegia
- Not reliable for drug dosing (eGFR is in ml/min/1.73m^2)
- Not reliable in pregnancy
- Not valid in patients who are on medications that impair secretion of creatinine such as co-trimoxazole

MDRD: Modification of Diet in Renal Disease
eGFR: Estimated glomerular filtration rate

It is imperative to identify CKD patients early so that interventions that improve CV mortality and morbidity and delay progression of CKD can be implemented in a timely manner.

Recently, cystatin C, a low molecular weight protein, has been shown to predict GFR reliably and has been shown to be a better predictor of CV mortality as well as progression to end stage renal disease. It is still quite costly for routine clinical use but its future looks bright.

It has to be noted that screening for CKD does not depend only on eGFR but also on evidence of kidney damage. Thus, when screening for CKD, not only should a clinician request an eGFR but also look for kidney damage by requesting quantification of protein in urine and, in selected cases, ultrasound of the kidneys. Proteinuria is the single most powerful predictor of end stage renal disease. Traditionally, proteinuria was measured by 24 hour urine collection but this test is cumbersome for patients and prone to collection errors. For screening simply requesting an albumin to creatinine ratio and in patients with gross proteinuria, a protein to creatinine ratio gives good estimate of 24 hour urine protein excretion. If the units of measurement for protein is g/L and for creatinine is mmol/L then simply multiplying the ratio by 10 would give a good estimate of the 24 hour urine protein excretion in g/day.

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