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Demystifying chronic kidney disease: Clinical caveats for the family physician

Primary care physicians play an essential part in managing patients with chronic kidney disease by helping them meet care objectives and providing ongoing medical care and support through all stages of kidney disease.

ABSTRACT: The number of patients with chronic kidney disease in BC is growing. There is a common misconception that patients with kidney diseases have complex medical problems that can only be managed by specialists. However, with the introduction of lab reporting of kidney function, publication of practice guidelines, and continuing medical education opportunities, a shared-care approach involving the family physician and specialists is being fostered in this province, with resulting improved patient outcomes. The family physician has an important role to play regarding diagnosis, interpretation of kidney function tests, and meeting care objectives (e.g., blood pressure and blood sugar control). Regular assessment for cardiovascular disease and conditions related to chronic kidney disease is also essential. Once patients are undergoing dialysis or if they choose palliative care, a collaborative approach between the family physician, nephrologist, and renal team (dialysis nurses, dietitians, pharmacists, and social workers) provides the best care for these patients.

Chances are you have several patients in your practice with chronic kidney disease (CKD). In BC, there are at least 145 000 people with an estimated glomerular filtration rate (eGFR) of less than 60 mL/min, and about 35 000 people whose physicians have actually identified CKD as a medical problem. However, if you also include those at highest risk for CKD (people with cardiovascular disease, diabetes, or both), this number could be as high as 400 000. In contrast, only 2000 or so patients are on dialysis (hemodialysis or peritoneal dialysis), and there is an equally small number who have received kidney transplants.[1] The main reason for this discrepancy is the high cardiovascular mortality rate associated with CKD: many patients die before they reach the point where they require dialysis.[2] In addition, a significant proportion of patients have stable, nonprogressive CKD.

Given that mortality increases exponentially as GFR declines,[3] we may be able to improve outcomes if we can halt or significantly delay the progression of CKD. This requires improving communication between family physicians, nephrologists, and other specialists, identifying CKD at earlier stages, and using a collaborative approach to care for these patients. The BC guidelines on CKD[4] provide detailed information for family physicians and expand on the management issues reviewed here.

What is chronic kidney disease?

Chronic kidney disease is defined as an eGFR < 60 mL/min that is present for 3 or more months, or evidence of kidney damage at any level of GFR.[5] Kidney damage may manifest in several ways, including abnormalities in serology, urinalysis (e.g., red cells, proteinuria), or imaging studies (e.g., polycystic kidneys). The abnormalities must be present for 3 or more months to ensure that acute reversible events are not the cause of the low

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GFR or urine abnormalities (e.g., acute renal failure in the setting of intravascular volume depletion or urinary tract infection).

Chronic kidney disease is staged according to the National Kidney Foundation recommendations.[5] **Table 1** lists these stages and several associated conditions that occur with increasing frequency, usually in the more advanced stages of CKD (occasionally Stage 3, more commonly Stages 4 and 5).[6,7] It is important to note that patients with an eGFR ≥ 60 mL/min who do not have any blood or urine abnormalities, nor structural abnormalities on ultrasound imaging, do not have kidney disease. Only those with an eGFR ≥ 60 mL/min and one or more of these abnormalities can be diagnosed with Stage 1 or 2 CKD. This common misconception has led to unnecessary anxiety and investigation of otherwise well people.

Table 1. Stages of chronic kidney disease.

Stage	Description	eGFR (mL/min)	Potential complications of reduced GFR (in alphabetical order)
1	Kidney damage with normal or ↑ GFR	≥90	• Anemia, including functional iron deficiency • Blood pressure increases • Calcium absorption decreases • Dyslipidemia /heart failure/volume overload • Hyperkalemia • Hyperparathyroidism • Hyperphosphatemia • Left ventricular hypertrophy • Metabolic acidosis • Malnutrition potential (late)
2	Kidney damage with mild ↓ GFR	60–89	
3	Moderate ↓ GFR	30–59	
4	Severe ↓ GFR	15–29	
5	Kidney failure	<15 or dialysis	

Source: Adapted from Identification, Evaluation and Management of Chronic Kidney Disease (www.health.gov.bc.ca/gpac/pdf/ckd.pdf)

Who should be screened for CKD?

There are several groups at high risk for CKD. These include those with diabetes, hypertension, cardiovascular disease, a family history of kidney disease, and those belonging to specific high-risk ethnic groups: people of First Nations, Pacific Islands, African, and Asian descent (**Table 2**). In general, these high-risk groups should be screened every 1 to 2 years using serum creatinine and spot urine tests. Diabetics should be screened on a yearly basis. Although age over 60 is associated with an increased risk of kidney disease, in the absence of one of the high-risk features listed in **Table 2**, routine screening based solely on advanced age is not recommended.

Table 2. Common risk factors for CKD that should prompt screening.

- Diabetes
- Hypertension
- Cardiovascular disease
- Family history of kidney disease
- Ethnicity: First Nations, Pacific Islands, African, and Asian

How do I screen high-risk patients for CKD?

Kidney function studies, urinalysis, and albumin/creatinine ratio (ACR) testing are the primary screening methods. The eGFR is the best laboratory marker for kidney disease and is computed from the serum creatinine value in most laboratories in British Columbia. Persistent eGFR < 60 mL/min indicates a substantial reduction in kidney function. In an otherwise stable patient who is found to have an eGFR < 60 mL/min, this test should be repeated monthly for 2 to 3 months to assess for chronicity. In addition, spot urine tests should be conducted as indicated below.

Spot urine tests, including a urinalysis and albumin/creatinine ratio test, should be performed to screen for CKD. A urinalysis investigates for abnormalities such as white or red blood cells. If persistently present, these abnormalities are suggestive of underlying kidney disease. If a cellular cast is observed, this is always pathologic and confirms kidney disease (e.g., glomerulonephritis, interstitial nephritis). A persistently elevated albumin/creatinine ratio greater than 2.0 mg/mmol in males and greater than 2.8 mg/mmol in females is indicative of microvascular disease, glomerular disease, or both. If the ACR is found to be elevated, testing should be repeated on at least two subsequent occasions separated by 1 week to 2 months to confirm a persistent abnormality. The presence of an elevated ACR (and not the absolute value) is what matters.

If a diagnosis of CKD is established, an assessment for progression and conditions associated with CKD should be performed as described below.

What aspects of the eGFR calculation should I keep in mind?

Low eGFR does not always indicate the presence of kidney disease. Below are some factors unrelated to kidney disease that may lead to an eGFR < 60 mL/min.[8]

Age: Glomerular filtration rate declines with age. A rule of thumb is that the GFR stays within the normal range (~100 mL/min) until the age of 40, and then declines at approximately 10 mL/min per decade, so that at age 80, normal GFR is 60 mL/min. Since the accuracy of the equation used to estimate GFR (the modified MDRD formula) in those older than 75 is questionable[9] (and in those over the age of 85 even more questionable), and may underestimate true kidney function, eGFR values between 45 and 60 mL/min may not actually reflect true kidney disease in the absence of other blood, urine, or structural abnormalities. In the absence of these abnormalities, we recommend that patients with these values do not need consultation with specialists unless there is a progressive decline in kidney function. If you are unsure whether to refer a patient, most specialists are happy to answer questions by phone.

Only those with an eGFR ≥60 mL/min and urine and/or structural abnormalities can be diagnosed with Stage 1 or 2 CKD.

Body habitus: In the absence of kidney disease, a patient's serum creatinine reflects their body size, and more specifically muscle mass. Thus a person of small stature or lower total body muscle mass can be expected to have a lower serum creatinine value, and a larger individual of higher total body muscle mass can be expected to have a higher serum creatinine value. For example, a 70-year-old female of European descent who is 1.63 m tall (5'4"), and weighs 50 kg (110 lb) with a BMI of 18.9 would be expected to have a serum creatinine of approximately 70 μmol/L, which would translate into an eGFR of 72 mL/min. This is normal in the absence of any urinary or structural abnormalities of the kidneys. However, if the woman's serum creatinine were 110 μmol/L, this would correspond to an eGFR of 43 mL/min and indicate Stage 3 CKD.

This caveat also applies to people who have lost limbs, have disorders associated with muscle wasting or atrophy, or those who have been bedridden for a prolonged time. In these groups, the serum creatinine value is lower than expected for body size given the loss of muscle mass, and this must be taken into consideration when interpreting serum creatinine and eGFR. Obesity does not affect the serum creatinine or eGFR measurement.

Gender and ethnicity: In general, women have a lower serum creatinine than men of the same size and age. People of African descent tend to have higher serum creatinine levels when compared with people of European descent of the same size, while people of Asian and Hispanic descent tend to have lower serum creatinine levels. The equation as currently calculated in the labs does not take ethnicity into account. Contact a specialist if you are not certain about how to interpret the results.

Diet, hydration status, and medications: The eGFR calculation is not accurate in people on special diets (e.g., very high or low in protein). Likewise, an individual should be in stable condition and a well-hydrated state when screening tests are performed since an altered hydration status will also affect serum creatinine, and thus the eGFR. Finally, these screening tests should not be performed while a patient is on certain medications that interfere with secretion of creatinine, such as trimethoprim, cimetidine, sulfamethoxazole, ciprofloxacin, or fenofibrate.

What should I do if my patient has established CKD?

Once screening tests have confirmed a diagnosis of CKD, the next steps in management include determining the stage of CKD and the underlying cause, assessing the need for specialist referral, and identifying care objectives for the CKD patient.

Staging: The stage of CKD is determined from the National Kidney Foundation guidelines (**Table 1**).[5] Patients with an eGFR ≥ 60 mL/min with no blood, urine, or structural abnormalities do not have kidney disease. Only those with an eGFR ≥ 60 mL/min and urine and/or structural abnormalities can be diagnosed with Stage 1 or 2 CKD.

Etiology: The cause of kidney disease is often multifactorial, especially in the high-risk population with underlying hypertension, diabetes, or cardiovascular disease. In a patient with these comorbidities, a persistent eGFR < 60 mL/min with minimal proteinuria and normal sized kidneys on ultrasound is often assigned a diagnosis of microvascular kidney disease or ischemic nephropathy, reflecting multiple processes culminating in CKD. Not all patients need an ultrasound if there is little question about the possible contributors to reduced kidney function.

A renal ultrasound can sometimes be helpful in determining the underlying cause of kidney disease. While the renal ultrasound is diagnostic for a few kidney diseases (e.g., polycystic kidney disease, obstruction, stones), the ultrasound results are often normal. Renal ultrasound can be suggestive of underlying renal artery stenosis if differential kidney size is observed, and nonreversibility of reduced kidney function is virtually confirmed when small kidneys are seen.

What do I need to pay attention to in patients with CKD?

The following care objectives should be considered for patients with CKD. Clinicians should refer to the official BC guidelines on CKD for more detailed information.[4]

Blood pressure: Blood pressure should be measured at every visit, with a goal of BP < 130/80 in all patients with CKD. An angiotensin converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) are recommended as first-line therapy, and can be combined with close monitoring of serum creatinine and potassium to achieve BP and proteinuria goals. Most patients with CKD will require more than two drugs to control BP.[10] It is important to be sure that patients are euvolemic, that is, not volume contracted, when started on an ACEI or an ARB.

eGFR: Kidney function should be measured at least every 6 months, with any change in patient status, and with the addition of medications that can affect kidney function. For example, serum creatinine and potassium levels should be measured within 2 weeks after initiation or dose-titration of an ACEI or ARB. If a rise in serum creatinine of more than 20% or a fall in eGFR of more than 15% is observed, further measurements should be performed within 1 or 2 weeks. Often the kidney function stabilizes; if not, further consultation is warranted. Of note, acute renal failure precipitated by an ACEI or ARB may indicate underlying renal artery stenosis; this is often accompanied by very good blood pressure control, and in the absence of other renal insults, referral to a specialist should be considered.

ACR: The patient's albumin/creatinine ratio should be measured every 6 to 12 months with a goal of reducing protein excretion by 50% or more from baseline. While the number is not always consistent, it is the trend that is important.

Cardiovascular disease risk: Assessment for cardiovascular disease risk should be performed in all patients with CKD and managed in accordance with relevant guidelines.[11] Lipid profiles should be measured at least annually, and more often in those on therapy. In those younger than 70, dyslipidemia should be aggressively treated with a goal of LDL < 2.5 mmol/L, and of TC/HDL < 4.0. Currently, evidence for lipid targets is lacking in those older than 70. In diabetics, measure blood glucose every 3 months with a target of HbA1c ≤ 7.0%. Be aware that long-acting sulfonyureas may be associated with hypoglycemia in patients with a GFR < 60 mL/min. If this occurs, use a short-acting or non-sulfonyurea agent. Encourage your patients with CKD who smoke to stop, and provide support when they are receptive to this idea. Counsel your CKD patient to maintain a healthy lifestyle, adequate nutrition, and normal BMI. You should also encourage patient self-management, as patients with kidney disease have better outcomes if they take an active role in their care.

Conditions associated with CKD: Patients should be assessed for anemia, abnormalities of mineral metabolism, and malnutrition. A hematology profile (hemoglobin and transferrin saturation), mineral metabolism parameters (calcium, phosphate, and intact parathyroid hormone), and nutrition profile (albumin) should be measured at least annually, or more frequently with advanced kidney disease. The goals of therapy for hemoglobin is a normal range for gender (if not on erythropoietin therapy), and 110 g/L to 125 g/L if on erythropoietin therapy. In BC currently, ordering these expensive medications is restricted. Importantly, the majority of patients with lower eGFR values have a relative iron deficiency leading to anemia, thus it is reasonable to initiate iron therapy if transferrin saturation is less than 20% (e.g., ferrous fumarate up to 900 mg p.o. daily). It is important to note that ferritin can be misleading; it's an expensive test and not routinely recommended in CKD patients to assess iron stores. The goals of therapy for mineral metabolism and nutrition are to keep the associated laboratory parameters within a normal range.

Immunizations: Patients with CKD should receive influenza vaccine (annually), and pneumoncoccal vaccine (every decade). If the patient is being considered for dialysis, immunization against hepatitis B is recommended as response to this vaccine is more predictable at a higher level of GFR.[12]

Exposure to nephrotoxic medications: Aminoglycosides, nonsteroidal anti-inflammatories, and COX-2 inhibitors should be avoided in those with CKD Stage 3 or greater. These medications should also be used with extreme caution in patients with Stage 1 or 2 CKD. Intravenous or intra-arterial

radiocontrast use poses a risk of acute kidney injury in patients with CKD Stage 3 or greater. If imaging is required, an alternative imaging technique (e.g., MRI) should be used, or the patient should be given protection with IV hydration (or perhaps N-acetylycysteine[13]) according to an established protocol,[14] or in consultation with a nephrologist. Finally, the dose of any medication that is renally excreted (e.g., allopurinol, digoxin, lithium) should be appropriately adjusted to the patient's level of kidney function.

Depression and grief reaction: Patients with chronic disease, including CKD, commonly experience depression and grief. It is important to identify and address psychosocial issues when they arise and provide support to the patient.

Does my patient with CKD have stable or progressive disease?

Many patients with CKD have nonprogressive disease. The best indicator of renal prognosis for most is their eGFR values over time. Other clinical indicators of a good prognosis are minimal to no proteinuria (e.g., ACR < 30 mg/mmol corresponding to urinary protein < 0.5 g/day), good BP control, and those who easily meet care objective targets. Slow progression or nonprogression is often observed in patients older than 75 with CKD.[15] For example, if an 85-year-old hypertensive female has a persistent eGFR of 35 mL/min over 6 to 12 months with a normal urinalysis, an ACR of 4 mg/mmol, and controlled BP, it is unlikely that her renal disease will progress. There are some kidney diseases (e.g., polycystic kidney disease, diabetic nephropathy) that have unpredictable progression patterns, even when all risk factors and conditions associated with CKD are well controlled.

When do I refer my patient to a specialist?

Referral to a specialist (nephrologist or internist) is recommended for acute causes of renal failure (e.g., vasculitis, lupus) that are often associated with an active urinary sediment, rapid sustained decline in renal function, sudden or severe onset of symptoms (e.g., hypertension, edema), or constitutional symptoms. In addition, those patients with structural abnormalities on imaging or a known family history of kidney disease should be referred.

In patients with CKD, specialist referral is recommended when patients have eGFR < 30 mL/min, or when eGFR declines by more than 10% to 15% annually, indicating progressive CKD. Referral can be considered in earlier stages of CKD if urine protein increases over time despite appropriate therapy, or if a large amount of protein excretion (ACR > 60 mg/mmol) or an abnormal urinalysis is found on initial screening tests. In addition, specialist referral can be considered if there is difficulty controlling the conditions associated with CKD (e.g., hypertension, anemia). It is important to remember that preparing a patient for renal replacement therapy requires a minimum of 1 year, thus early referral is essential.[16] If there are questions about the appropriateness of the referral, please contact your local specialist directly.

Urology consultation should be considered if initial imaging demonstrates stones or obstruction, the patient has a history of nephrolithiasis, or a patient in the earlier stages of CKD (Stages 1 and 2) has isolated microscopic hematuria, even if the renal ultrasound is normal. This is especially important in smokers and those older than 40, as these patients often require cystoscopy to rule out occult bladder malignancies.

What role do I play once my patient starts dialysis?

It is a common misconception that patients on dialysis have medical issues beyond the scope of a family physician's practice. These patients suffer from common medical conditions similar to the rest of the population and should be seen at least yearly by their family physician for a periodic health exam. They should undergo age-appropriate screening (e.g., mammography, colonoscopy, PSA) and immunizations, and be reviewed as needed for any primary care issues. The focus of the nephrologist at this stage is to ensure the patient is receiving adequate dialysis and to manage the associated conditions of kidney disease (hypertension, anemia, mineral metabolism, and malnutrition). The nephrologist and renal team (dialysis nurses, dietitians, pharmacists, and social workers) are also focused on the overall well-being of the patient and will help manage any acute issues that arise. Ideally, a shared-care approach involving the nephrologist and renal team and the family physician should be fostered to provide the best patient care.

What role do I play if my patient chooses palliative care?

A patient with CKD may choose not to start dialysis, and opt for conservative therapy. It is especially important for the family physician to play a primary role in this setting as the patient often has a long-standing relationship with this individual. The nephrologist and renal team will often remain actively involved in the care of the patient to help manage symptoms and signs of end-stage renal disease, such as volume overload and electrolyte

abnormalities. In addition, members of the renal team (especially social workers) can help provide support to the patient and family, and assist with end-of-life planning in conjunction with the family physician. Again, communication and collaboration between the nephrologist, the renal team, and the family physician are essential to provide the best care to these patients.

Summary

Increased recognition of CKD has been fostered by laboratory reporting of eGFR, publication of CKD practice guidelines, and improved CKD-related CME for primary care physicians. Many patients have nonprogressive disease and require attention to the usual problems of cardiovascular disease risk reduction, blood pressure control, and blood sugar control.

If you want to learn more about the physician's role in CKD management, consider attending BC Nephrology Days, 2–3 October 2008, where there will be a specific stream of talks on 3 October to further educate general practitioners about treating patients with CKD. Please visit the BC Renal Agency web site (www.bcrenalagency.ca) for more details.

Competing interests

None declared.

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