An approach to treating older adults with chronic kidney disease

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Chronic kidney disease (CKD) in older adults is a worldwide epidemic that affects nearly 40% of people aged 65 or older.¹ In the United States, CKD in people aged 65 years and older is more common (38%) than in all other age groups.¹ Over the last 4 decades, patients older than 75 years are the fastest-growing group to start dialysis.¹ In Canada, more than half of patients starting dialysis are 65 years or older.² Chronic kidney disease confers considerable morbidity on patients and consumes a substantial amount of health care resources.¹ Few evidence-based guidelines specifically speak to management of CKD in older adults, many of whom are frail and have multiple comorbidities,³ and physicians should exercise caution when extrapolating general guidelines to older adults. We discuss the causes and consequences of CKD through a geriatric lens, and outlines principles of best practice. The evidence underpinning this review is summarized in Box 1.

What are the causes of kidney dysfunction in older adults?

Chronic kidney disease in patients older than 65 years⁴ is defined by an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/m².⁴ However, a physiologic decline in GFR of about 8 mL/min per decade begins around the fourth decade of life.⁵ Physiologic CKD usually does not lead to end-stage kidney disease (ESKD), which is defined by the development of uremic symptoms or need for renal replacement therapy. A hallmark of age-related kidney decline is the absence of proteinuria,⁶ which portends a favourable prognosis. The rate of eGFR decline can also be instructive; most older patients have stable eGFR trends,⁷ and patients with slow eGFR decline (< 2 mL/min/yr) and minimal proteinuria (albumin-to-creatinine ratio [ACR] < 3 mg/mmol)⁸ are unlikely to reach ESKD.⁷

Older adults are at higher risk of acute kidney injury (AKI) from nephrotoxic medications, volume depletion, urinary tract obstruction and acute illnesses including sepsis and acute cardiovascular events.⁹ Nonsteroidal anti-inflammatory drug (NSAID) use is a risk factor for AKI and CKD.¹⁰ Topical NSAIDs at lower potencies may be safer to use in patients with CKD, although systemic absorption in older frail patients with low muscle mass may occur.¹¹ Finally, systemic diseases can cause kidney dysfunction, including plasma cell dyscrasias (e.g., multiple myeloma), drug-induced interstitial nephritis and anti-neutrophilic cytoplasmic antibody vasculitis, the most common glomerulonephritis in older adults.¹²

How should clinicians investigate kidney dysfunction?

A current (2018) Canadian guideline recommends ordering eGFR and ACR to screen for kidney disease annually in high-risk populations such as those with hypertension, type 2 diabetes mellitus or cardiovascular disease.¹³ Screening older patients who do not have risk factors is not recommended.¹³

Key points

- Chronic kidney disease (CKD) in older adults can result from a combination of physiologic, age-related decline in kidney function, renocardiovascular risk factors and external insults.
- The management of risk factors for CKD should be individualized with consideration of less aggressive targets for frail patients at risk of polypharmacy.
- The Kidney Failure Risk Equation is a useful tool in the evaluation of and ongoing treatment for CKD for both general practitioners and nephrologists.
- Clinicians should have open discussions with their older patients with CKD regarding their goals of care and the potential benefits and harms of renal replacement therapy.

Box 1: Evidence used in this review

We conducted a targeted search of MEDLINE to identify original research and review articles on chronic kidney disease in older adults published from January 2000 through March 2022. Medical subject heading search terms included “elderly,” “geriatrics,” “advance care planning,” “chronic kidney disease,” “blood pressure” and “management.” In addition, we reviewed current European, American and Canadian guidelines on the management of chronic kidney disease and hypertension including Kidney Disease: Improving Global Outcomes, Hypertension Canada 2017, and American Society Nephrology Geriatric Nephrology Curriculum.
In a patient presenting with new or worsening kidney dysfunction, additional tests should be ordered as indicated (Table 1). These may include a urinalysis and an abdominal ultrasound. Appropriate medications should be held (Table 2), particularly in the presence of relative hypotension. Nephrology consultation should be sought if a readily reversible cause of AKI or CKD is not discovered.

In older patients, physiologic CKD should be distinguished from pathologic causes of CKD, such as systemic diseases (cardiovascular disease, diabetes, hypertension, autoimmune diseases) or external insults. A sudden decline in eGFR (e.g., a more than 1.5-times increase from baseline creatinine) over a short period (days to weeks), especially when associated with hematuria and proteinuria, may be suggestive of glomerulonephritis. Low urine sodium is an excellent test of volume depletion, although it can be falsely negative in patients on diuretics. Patients with established CKD should have serum creatinine, eGFR, ACR and electrolytes measured routinely (Table 1). The frequency of investigations is dictated by the stage and stability of the CKD.

### Table 1: Investigations to assess kidney dysfunction

<table>
<thead>
<tr>
<th>Test</th>
<th>Notes</th>
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<tbody>
<tr>
<td><strong>Recommended investigations annually for CKD stage 2–3</strong></td>
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</tr>
<tr>
<td>Creatinine, eGFR</td>
<td>Rapid or progressive worsening in days to weeks suggests an active potentially reversible process.</td>
</tr>
<tr>
<td>Electrolytes (Na, K, Cl, CO₂)</td>
<td>Target bicarbonate level ≥ 22 mmol/L, K ≤ 5.4 mmol/L.</td>
</tr>
<tr>
<td>ACR</td>
<td>Should be ordered routinely for patients with CKD, alongside creatinine and eGFR. Important component of KFRE score.</td>
</tr>
<tr>
<td><strong>Recommended investigations for AKI or de novo CKD (in addition to above tests)</strong></td>
<td></td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Can help determine renal cause for CKD (e.g., glomerulonephritis, acute interstitial nephritis). Note that dipstick protein identifies only albumin and not free light chains. May miss cast nephropathy</td>
</tr>
<tr>
<td>ACR</td>
<td>Should be ordered routinely for patients with CKD. Important component of KFRE score.</td>
</tr>
<tr>
<td>Urea</td>
<td>Useful for determining volume depletion. May be elevated in gastrointestinal bleeds or in patients taking steroids.</td>
</tr>
<tr>
<td>Urine electrolytes</td>
<td>Low urine Na (FENA &lt; 1%) is consistent with intravascular volume depletion (unreliable in context of diuretic use).</td>
</tr>
<tr>
<td>Ultrasound of kidneys</td>
<td>Assesses for structural disease (cysts, congenital abnormalities, hydronephrosis) and renal stones. Small atrophic kidneys can be suggestive of long-standing, irreversible CKD. Consider renal Doppler to rule out renovascular disease if patient presents with marked hypertension or difference in kidney size.</td>
</tr>
<tr>
<td>Serum protein electrophoresis</td>
<td>To identify plasma cell dyscrasia (e.g., multiple myeloma), particularly important in patients who have new, unexplained anemia or hypercalcemia.</td>
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<tr>
<td>24-hour urine protein and urine electrophoresis</td>
<td>Important to do if ACR &gt; 300 mg/mmol (&gt; 3 g/d).</td>
</tr>
<tr>
<td>Creatine kinase levels</td>
<td>May suggest rhabdomyolysis (e.g., patients recently started on statins with myopathy).</td>
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<tr>
<td>Antineutrophil cytoplasmic antibody serology</td>
<td>Should be ordered if urinalysis shows blood and protein and rapidly rising creatinine.</td>
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<tr>
<td>CBC with blood film</td>
<td>Fragments on blood smear and/or low platelets suggest thrombotic microangiopathy (thrombotic thrombocytopenic purpura, HUS or aHUS).</td>
</tr>
<tr>
<td><strong>Recommended tests every 3–6 months for patients with CKD stage 4–5</strong></td>
<td></td>
</tr>
<tr>
<td>Creatinine, eGFR</td>
<td>Rapid or progressive worsening in days to weeks suggests an active reversible process.</td>
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<td>Urea</td>
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<td>Electrolytes (Na, K, Cl, CO₂)</td>
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</tr>
<tr>
<td>Calcium panel (Ca, PO₄, Mg, albumin, PTH)</td>
<td>Target a PTH &lt; 3 times the upper limit of normal for patients with CKD stage 4 and 5.</td>
</tr>
<tr>
<td>ACR</td>
<td>To convert ACR to 24-h albuminuria, multiply by 10 for women and by 15 for men. Important for calculation of KFRE.</td>
</tr>
<tr>
<td>CBC, ferritin, transferrin saturation</td>
<td>Ferritin may be elevated in CKD or AKI. Ferritin &gt; 200 µg/L or transferrin saturation &lt; 20% suggests iron deficiency.</td>
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Note: ACR = albumin-to-creatinine ratio, aHUS = atypical hemolytic uremic syndrome, AKI = acute kidney injury, Ca = calcium, CBC = complete blood count, CKD = chronic kidney disease, Cl = chloride, CO₂ = bicarbonate, eGFR = estimated glomerular filtration rate, FENA = fractional excretion of sodium, HbA₁c = glycated hemoglobin percentage, HUS = hemolytic uremic syndrome, K = potassium, KFRE = Kidney Failure Risk Equation, Mg = magnesium, Na = sodium, PO₄ = phosphate, PTH = parathyroid hormone.
Can development of ESKD be predicted?

An important challenge facing physicians is to identify patients at high risk of CKD progression who would benefit from intensive risk factor control. Stage of CKD (Box 2) alone is a poor discriminant of progression. Creatinine-based eGFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) model has several drawbacks: it is affected by age, sex and muscle mass. It also uses a race coefficient, and will eventually be supplanted by a race-independent refitted model that is more accurate, a change based on race being recognized as a social rather than biological construct.

Adding ACR to eGFR improves prognostication and has led to a paradigm shift, ushered in by the development of an internationally validated risk prediction model known as the Kidney Failure Risk Equation (KFRE). The KFRE predicts 2- and 5-year risk of ESKD using 4 variables: age, gender, eGFR and ACR (online calculator available at https://kidneyfailurerisk.com/). Generalists can use KFRE scores to identify patients with CKD who are at higher risk of progression and who should be referred to nephrology. For example, the Ontario Renal Network suggests that people with a 5-year KFRE score greater than 3%-5% may benefit from a nephrology referral.

Kidney Failure Risk Equation scores help generalist physicians balance cardiovascular risk factor control with the risk of polypharmacy. The KFRE promotes an individualized approach in frail individuals; those with low-risk KFRE scores may not require strict blood pressure, lipid and glycemic control specifically for renoprotection, thus potentially decreasing polypharmacy, the risk of falls and medication-related adverse effects such as AKI.

The KFRE has limitations: it may be less accurately predictive in patients with glomerulonephritis, or hereditary or structural diseases such as polycystic kidney disease. However, these conditions are less prevalent in older populations. The KFRE should not be used in patients with AKI or fluctuating eGFR.

Box 2: Chronic kidney disease stages, albuminuria categories and the components of the Kidney Failure Risk Equation (KFRE) score

Chronic kidney disease stages by GFR (mL/min/1.73 m²)

- G1 ≥ 90
- G2 60–89
- G3a 45–59
- G3b 30–44
- G4 15–29
- G5 < 15

Albuminuria category by urine (mg/mmol)

- A1 < 3
- A2 3–30
- A3 > 30

(Higher stages of chronic kidney disease, especially in conjunction with higher degrees of proteinuria, are associated with increased risk of end-stage kidney disease.)

KFRE score

The KFRE (available at https://kidneyfailurerisk.com/) provides further prognostic information by calculating the 2- and 5-year risk of developing end-stage kidney disease, using the 4 variables below. It should be specified whether the test was done in North America or elsewhere.

- Age
- Sex
- eGFR
- ACR

Note: A = albuminuria, ACR = albumin-to-creatinine ratio, G = GFR, GFR = glomerular filtration rate.

What are the risk factors for progressive CKD?

Factors associated with an accelerated rate of GFR decline include hypertension, hyperglycemia, atherosclerotic cardiovascular disease, smoking and previous episodes of AKI.
Blood pressure (BP), lipid and blood glucose control are the cornerstones of CKD management. Blood pressure control and albuminuria reduction are renoprotective; renin–angiotensin–aldosterone system (RAAS) blockade and sodium–glucose cotransporter 2 (SGLT2) inhibition are important for achieving these goals. However, guidelines do not agree regarding the optimal BP targets for older patients. Hypertension Canada (2020) recommends a target BP goal of less than 130/80 in patients with CKD and diabetes mellitus, and less than 120/80 in patients with CKD without diabetes mellitus, irrespective of age. These recommendations are based primarily on analysis of the Systolic Blood Pressure Intervention Trial (SPRINT), which included older patients, and the Hypertension in the Very Elderly Trial (HYVET), which included patients older than 80 years. The Kidney Disease: Improving Global Outcomes (KDIGO) international working group’s 2021 guidelines on hypertension recommended intensive BP lowering (systolic < 120 mm Hg), irrespective of diabetes status and age. Caution must be exercised in older adults; KDIGO guidelines acknowledge the limitations of evidence for BP lowering in patients older than 75 years. Individuals with substantial frailty who have a higher risk of postural hypotension and falls may benefit from more liberal BP targets. Post hoc analysis of the SPRINT trial showed a higher risk of adverse events in patients with lower diastolic BP.

Similarly, glycemic control should be based on patients’ characteristics. The 2018 Diabetes Canada guideline recommends that glycated hemoglobin (HbA1c) targets should be adjusted according to the level of frailty: aiming for HbA1c 7.1%–8.5% in patients with dementia is a reasonable strategy, with a focus on avoiding extremes in blood glucose levels. For most other older patients, the target should be HbA1c 7.5%–9.0%.

Statin use in older patients reduces cardiovascular events and mortality, but this effect is attenuated or even lost in those older than 85 years. If myopathies are identified, lower statin dosing should be considered. Given the potential musculoskeletal adverse effects of statins, it may be prudent to defer statin therapy in patients with poor nutrition who are already at risk of sarcopenia and falls.

Special considerations for older adults with CKD

Electrolyte management
Hyperkalemia is an important consideration in older patients with CKD, especially those on RAAS blockers. Potassium levels of 6.0 mmol/L or higher require urgent assessment and intervention. Potassium levels chronically between 5.4 and 6.0 mmol/L should prompt physicians to assess dietary potassium intake, adjust doses of RAAS blockers and consider oral potassium binders. Traditionally, sodium polystyrene sulfonate has been used to control potassium; however, these agents confer a small risk of gut necrosis, especially when combined with sorbitol. Recently, newer potassium binders (sodium zirconium cyclosilicate and patiromer) have become available in Canada, which have been shown to be safer and effective for potassium control, and may allow continuation of RAAS blockers while allowing for diet liberalization.

A common and treatable cause of hyperkalemia in older adults is constipation. Osmotic laxatives, such as lactulose and polyethylene glycol, are safe when used judiciously in such patients, and can help excrete potassium with or without added potassium binders. Sorbitol and phosphate-based enemas should be avoided, and magnesium-based laxatives should be used with caution, given the risk of hypermagnesemia. Newer agents such as secretagogues (linaclotide and lubiprostone) are less commonly used but are safe and effective in CKD and may help excrete phosphate as well.

Strategies such as dietary potassium restriction and diuretics can have considerable adverse effects in older patients. Restrictive diets can lead to malnutrition, and diuretics increase the risk of AKI from volume depletion and electrolyte abnormalities, including hyponatremia. In frail patients, consideration should be given to discontinuing RAAS blockers rather than adding medications to manage electrolyte abnormalities.

Anemia in CKD
Anemia is common in patients with advanced CKD (stages 4 and 5). Anemia of CKD is a diagnosis of exclusion and is caused by relative erythropoietin deficiency. Symptoms of anemia — such as fatigue, cognitive dysfunction and decreased exercise tolerance — may be more prominent in older patients. Iron deficiency is also common, owing to poor absorption and malnutrition. Identifying iron deficiency requires nuanced interpretation of ferritin and transferrin saturation (Table 1). Ferritin levels are often elevated in patients with CKD and have low sensitivity for ruling out iron deficiency. Iron should be supplemented as indicated. Nephrologists may initiate an erythropoietin-stimulating agent to target a hemoglobin range between 100 and 110 g/L. Higher targets may be aimed for in patients with limited survival, but this brings with it a small risk of thrombosis and stroke events.

Osteoporosis and bone health
Bone health is an important consideration for older adults with CKD. Patients with CKD stage 5 often have secondary hyperparathyroidism, contributing to an increased risk of fragility fractures. Evidence regarding the best method of vitamin D supplementation is unclear. Hyperphosphatemia in CKD is common, but phosphate reduction is controversial in older patients. Limiting protein intake can lead to poor nutrition and worsened frailty. Oral phosphate binders (e.g., calcium carbonate) may allow for liberalization of diet, but can increase pill burden and cause constipation. Use of antiresorptive therapy such as bisphosphonates or denosumab is relatively contraindicated and should be considered only with dose adjustment after discussions with nephrology and experts in osteoporosis.

Goals of care planning
Patients and families should receive sufficient education about the benefits and harms of dialysis and participate in a shared decision-making process. Goals of care for ESKD should incorporate the patient’s values and preferences.

Patients with ESKD develop uremic symptoms that include fatigue and volume overload. Kidney transplantation has substantial survival benefits in older patients but this may not be a viable option in frail patients with limited life expectancy.
Although dialysis may provide increased survival and symptom relief, the benefit is modest in older and frail patients, and dialysis can be associated with considerable reduction in independence and quality of life. In Canada, patients with ESKD who are older than 70 years have a 1- and 5-year survival of 76% and 28%, respectively. Older patients undergoing dialysis experience substantial symptom burden including fatigue, pain, muscle cramps, insomnia and cognitive impairment. Older, frail patients may better tolerate home-based modalities such as peritoneal dialysis, which is associated with less hypotension than hemodialysis, and can be provided with the help of home care nurses.

Conservative kidney management without dialysis is a reasonable course of care for patients with multiple comorbidities and high degree of frailty. The focus is on managing symptoms and avoiding invasive or uncomfortable therapies that offer minimal benefit in survival (Table 3). Using prognostic tools such as frailty scales can help identify patients who might benefit from conservative kidney management (Box 3). Developing partnerships with palliative care services can help with transitioning patients to end-of-life care as uremic symptoms worsen.

### Conclusion

Chronic kidney disease in the older-adult population is associated with substantial morbidity. A patient-centred approach is necessary to balance the benefits of cardiovascular optimization with the

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### Table 3: Suggestions for management of symptoms related to chronic kidney disease in older adults

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>Restrict salt and fluid consumption. Consider volume overload. Higher doses of furosemide may be required as GFR drops. Optimize anemia management.</td>
</tr>
<tr>
<td>Pain</td>
<td>Avoid oral NSAIDs. Topical agents may be used with caution. Acetaminophen may have limited efficacy. Neuropathic agents such as gabapentinoids (start gabapentin at 100 mg orally daily). Monitor for fall risk. Opioids may be used for unremitting pain. Hydromorphone is the preferred opioid (start with 0.5 to 1 mg orally every 4–6 h, as necessary). There is limited evidence for cannabinoid use in CKD.</td>
</tr>
<tr>
<td>Nausea</td>
<td>Treat constipation. Large meals and strong smells may be triggering. Metoclopramide (2.5 mg orally every 4 h, as necessary) and ondansetron (4–8 mg orally every 8 h, as necessary). Atypical antipsychotics such as olanzapine (2.5 mg orally every 4 h, as necessary) or low-dose haloperidol (0.5 mg orally every 4 h, as necessary) can be beneficial.</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Thick emollients should be first line for symptomatic relief. Patients should avoid hot showers or baths as they may exacerbate dryness of skin. Topical agents include camphor and menthol-based compounds and low-potency steroids. Capsaicin-based creams may be effective. Gabapentinoids and SSRIs at low doses may be helpful. Antihistamines should be avoided, but hydroxyzine may be used with caution (10 mg twice per day, as necessary). Ultraviolet-B therapy may be used (poor evidence).</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>Nonpharmacologic therapies include exercise, reducing caffeine and limiting fluid intake in the evening. Diuretics should be dosed earlier in the day (e.g., second dose of furosemide no later than 2 pm). Treat benign prostatic hyperplasia where applicable. Treat pain, restless leg syndrome and pruritus. Consider melatonin (initiate at 3 mg at night) and mirtazapine (initiate at 3.75 mg to 7.5 mg at night).</td>
</tr>
<tr>
<td>Restless leg syndrome or cramping or both</td>
<td>Manage modifiable factors such as iron deficiency and use of antidepressants and dopamine antagonists. Low-dose magnesium supplementation may be beneficial. Gabapentinoids (start gabapentin 100 mg orally at night and titrate up). Consider dopamine agonists such as pramipexole (0.125–0.25 mg orally three times daily, as necessary) or ropinirole (starting dose 0.25 mg/d).</td>
</tr>
<tr>
<td>Depression</td>
<td>Manage contributing symptoms (e.g., pain, insomnia, pruritus). Optimize social supports. Nonpharmacologic interventions include cognitive behaviour therapy and exercise. Dose-adjusted antidepressants such as mirtazapine may be effective.</td>
</tr>
</tbody>
</table>

Note: CKD = chronic kidney disease, GFR = glomerular filtration rate, NSAID = nonsteroidal anti-inflammatory drug, SSRRI = selective serotonin reuptake inhibitor.
Box 3: Approach to shared decision-making in older adults with advanced chronic kidney disease

Explore goals of care in chronic kidney disease
- Identify substitute decision-maker or power of attorney
- Explore goals, wishes, values
- Explore limitations
- Explore cultural context

Use prognostic tools
- Identify patients who may benefit from conservative management
  - Rockwood Clinical Frailty Scale
  - Palliative Performance Scale
  - Karnofsky Performance Status
- Surprise question: Would you be surprised if the patient were still alive in 6 months?

Disclose prognostic information to patients who may have limited benefit from dialysis (decreased quality of life, limited survival benefit)

Incorporate patient goals and values to outline a treatment plan, including
- Transplant
- Dialysis
  - Home options such as home hemodialysis and peritoneal dialysis
  - In-centre hemodialysis
- Conservative kidney management

Box 4: Unanswered questions
- What are the optimal blood pressure thresholds and targets for older frail patients with chronic kidney disease? Which antihypertensive medications should be first line in such patients?
- Is the Kidney Failure Risk Equation valid for adults older than 90 years?
- What are safe and effective options for symptom control for older patients with chronic kidney disease (e.g., pain, pruritus, sleep, fatigue, depression)?
- How can care providers (family doctors, geriatricians and palliative care specialists) best care for patients with end-stage kidney disease who choose conservative goals of care?

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3. Farrington K, Covic A, Nistor I, et al. Clinical Practice Guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR < 45 mL/min/1.73 m²); a summary document from the European Renal Best Practice Group. Nephrol Dial Transplant 2017;32:9-16.
Review


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