Chronic kidney disease in the elderly
Assessment and management

Richard KS Phoon

Background
A reduction in estimated glomerular filtration rate (eGFR), and/or the presence of proteinuria, are the predominant manifestations of chronic kidney disease (CKD), which is common in the elderly population.

Objective
This article outlines the clinical significance of CKD in the elderly and summarises recently updated recommendations for its assessment, staging and management.

Discussion
Most elderly patients with CKD present asymptomatically. Despite this, it is clinically significant as it is one of the most potent risk factors for cardiovascular disease. Even modest reductions in eGFR are associated with an increased prevalence of CKD-related complications such as anaemia and hyperphosphataemia. Early detection is an important strategy and should include all three components of the kidney health check (blood pressure measurement, a blood test for serum creatinine and eGFR, and a urine test for albumin:creatinine ratio). Treatment is guided by the patient’s stage of CKD, based on kidney function (eGFR) and kidney damage (degree of albuminuria), and control of blood pressure to recommended levels with appropriate medications. The majority of elderly patients with CKD will not ultimately require, or desire, renal replacement therapy and may be safely managed in general practice.

Keywords
kidney disease; elderly; renal insufficiency

Chronic kidney disease represents an emerging public health problem. It is one of the most potent risk factors for cardiovascular disease and contributes to around 15% of all hospitalisations and nearly 10% of all deaths in Australia. Chronic kidney disease is also accompanied by multiple other comorbidities: hypertension, anaemia, hyperparathyroidism, and renal osteodystrophy. Timely identification and management of CKD can slow its rate of progression and reduce cardiovascular risk by up to 50%. However, the assessment and management of CKD in elderly patients can be an area of uncertainty for general practitioners.

Age-related GFR decline or chronic kidney disease?
After the age of 30 years, glomerular filtration rate (GFR) progressively declines at an average rate of 8 mL/min/1.73 m² per decade. The Australian Diabetes, Obesity and Lifestyle (AusDiab) study suggests that over one-third of people over the age of 65 years have an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m². There is considerable debate regarding the significance of this age-related decline in kidney function, which has been variously attributed to the effects of hypertension, atherosclerosis, or other comorbidities such as cardiovascular disease. Recent evidence suggests that even very elderly patients (>80 years of age) with modest reductions in eGFR (45–59 mL/min/1.73 m²) have a higher prevalence of CKD-related complications compared to patients with an eGFR ≥60 mL/min/1.73 m². Furthermore, as eGFR declines below 60 mL/min/1.73 m², there is an appreciable, increasing incidence of cardiovascular events and mortality. As a result, age specific cut-points for CKD diagnosis and staging are not currently recommended.

Detection of chronic kidney disease
Most elderly people with CKD are asymptomatic. Whole population screening for CKD is not cost-effective. However, general practitioners should consider targeted testing of high risk groups. These include adults aged more than 60 years, especially those who are known to smoke, have a family history of CKD, or who suffer from diabetes, hypertension, obesity or established cardiovascular disease. People of Aboriginal or Torres Strait Islander origin may be screened from 30 years of age, as

CPD
there is a much higher incidence of CKD and progression to end-stage renal disease, with the largest relative difference being in the 45–65 years age group.\textsuperscript{15} Testing for CKD should comprise a serum eGFR measurement, urinary albumin:creatinine ratio (ACR) and blood pressure (BP) measurement.

Albuminuria, in people with or without diabetes mellitus, is ideally measured by a first void morning urine ACR.\textsuperscript{16} Transient elevations of urine ACR can be caused by diurnal variations in protein excretion, urinary tract infections, fluid overload or acute febrile illness, so a raised urine ACR should be confirmed on repeat measurement. Similarly, a minimum of three reduced eGFR measurements, over at least a 3 month period, is used to confirm a diagnosis of CKD. The presence of a rapidly declining eGFR may also occur in acute kidney injury (particularly secondary to drugs such as nonsteroidal anti-inflammatory drugs [NSAIDs]), and should be repeated within 14 days.

**New chronic kidney disease staging guidelines: importance of proteinuria**

A recent large, collaborative meta-analysis of general population cohorts (n=105 000 participants) suggests that both eGFR <60 mL/min/1.73 m\(^2\) and albuminuria >1.1 mg/mmol are independent predictors of mortality risk.\textsuperscript{17} National guidelines now therefore recommend that staging of CKD is based on the combined indices of kidney function (measured or estimated GFR), kidney damage (albuminuria) and underlying diagnosis (eg. stage 2 CKD with microalbuminuria secondary to diabetes kidney disease). Table 1 illustrates the staging of chronic kidney disease.

**Management**

The majority of patients with early CKD (kidney function stages 1–3) will not ultimately progress to end-stage kidney disease for consideration of renal replacement therapy (ie. dialysis or transplantation) and can be primarily managed in general practice. Assessment and management should be guided by the stage of CKD as outlined in Table 2.

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**Table 1. Staging of chronic kidney disease\textsuperscript{33}**

<table>
<thead>
<tr>
<th>Kidney function</th>
<th>GFR (mL/min/1.73 m(^2))</th>
<th>Normal (urine ACR mg/mmol)</th>
<th>Microalbuminuria (urine ACR mg/mmol)</th>
<th>Macroalbuminuria (urine ACR mg/mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male: &lt;2.5</td>
<td>Female: &lt;3.5</td>
<td>Male: 2.5–25</td>
</tr>
<tr>
<td>1</td>
<td>≥90</td>
<td>Not CKD unless haematuria, structural or pathological abnormalities present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>60–89</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>45–59</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3b</td>
<td>30–44</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15–29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>&lt;15 or on dialysis</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Initial assessment is aimed at establishing the cause of CKD (Table 3), quantification of urine protein excretion, identification of any causes of reversible or treatable kidney dysfunction, assessment of cardiovascular risk and evaluation of any complications of CKD. A thorough medication history is important, as many medications may need to be ceased or reduced in the setting of CKD (Table 4). Investigations that may be considered include serum biochemistry (hyperkalaemia, hyperphosphataemia, hypocalcaemia and acidosis), blood count (anaemia), urinalysis (haematuria), urine ACR and urinary tract ultrasound (lower urinary tract obstruction, renal size and loss of corticomedullary differentiation). Examination of the urinary sediment may be helpful for the identification of red blood cell morphology (a high proportion of dysmorphic red blood cells suggests glomerular haematuria) or cellular casts (red cell casts suggest an active glomerulonephritic process). However, there are practical constraints, as a urine sample ideally needs to be centrifuged and examined less than 1 hour following collection.

**Hypertension in chronic kidney disease**

Reducing BP with appropriate medications to below target levels is one of the most important goals of CKD management. Angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blockade (ARB) therapy reduce albuminuria and retard the progression of CKD, particularly in patients with established diabetic kidney disease.\textsuperscript{18–20} ACEI or ARB therapy may be effective, even in patients with severe CKD,\textsuperscript{21} however, such treatment can be associated with an unacceptable fall in eGFR or rise in serum potassium. Serum biochemistry should be rechecked 1–2 weeks after initiation of treatment. A serum potassium level <6 mmol/L and an acute decline in eGFR no more than 25% below baseline that stabilises within 2 months are acceptable. Most patients require multiple anti-hypertensive agents. Recent studies suggest not only the absence of a clinical benefit of dual blockade (ACEI together with ARB) therapy over monotherapy but also an increase in adverse events.\textsuperscript{22} By comparison, several studies demonstrate efficacy of combining...
Iron deficiency is common in CKD and supplementation with oral or intravenous iron is required. When other causes of anaemia have been excluded or managed, erythropoietin stimulating agents may be considered where haemoglobin is under 100 g/L.

The decline of renal function leads to higher serum phosphate levels and lower calcitriol production. This is often combined with lower calcium absorption in the gastrointestinal tract. The resultant secondary hyperparathyroidism is associated with an increased risk of fracture and cardiovascular mortality.

Vitamin D supplementation suppresses the development of secondary hyperparathyroidism. However, cholecalciferol requires sufficient renal function, and calcitriol is preferred in later stages. Phosphate binders, such as calcium carbonate, are commonly titrated to the serum phosphate. Parathyroid hormone levels should be kept between 2–9 times the upper limit of normal.

### Nephrologists and multidisciplinary care

Referral to a specialist renal service may be considered when the cause of renal impairment is not clear or is rapidly progressive, in the presence of glomerular haematuria with macroalbuminuria, or when hypertension is difficult to control despite multiple agents. Specialist renal services also provide education for patients, often involving specialised nursing staff, social workers and dieticians.

A nephrologist should be considered at least 12 months before the anticipated commencement of dialysis or kidney transplantation.

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**Table 2. Guidelines for the management of chronic kidney disease**

<table>
<thead>
<tr>
<th>Colour code</th>
<th>Clinical action plan</th>
<th>Monitoring</th>
</tr>
</thead>
</table>
| **Yellow**  | • Investigations to exclude treatable kidney disease (eg. urinary tract infection or obstruction)  
• Reduce progression of kidney disease (especially by controlling BP to recommended levels with ACEI or ARB therapy)  
• Reduce cardiovascular risk  
• Avoidance of nephrotoxic medications and volume depletion  
• BP reduction (maintain BP consistently ≤140/90 or ≤130/80 if diabetes or albuminuria are present)  
• Lipid-lowering treatment (target total cholesterol <4.0 mmol/L and LDL-cholesterol <2.5 mmol/L)  
• Glycaemic control, if diabetic (target HbA1c <7.0%) | • 12 monthly clinical review  
• Clinical assessment  
  – BP  
  – weight  
  – fluid status  
• Laboratory assessment  
  – urine ACR  
  – electrolytes, urea and creatinine (eGFR)  
  – HbA1c (if diabetic)  
  – fasting lipids |
| **Orange**   | As for ‘yellow’ clinical action plan plus:  
• Early detection and management of CKD complications  
• Avoid renally-excreted medications  
• Adjust medication doses for kidney function  
• Appropriate referral to a nephrologist where indicated | • 3–6 monthly clinical review  
• As for ‘yellow’ clinical action plan plus:  
  – full blood count  
  – calcium and phosphate  
  – parathyroid hormone |
| **Red**      | As for ‘orange’ clinical action plan plus:  
• Appropriate referral to a nephrologist where indicated  
• Assess suitability and prepare for dialysis or pre-emptive transplant if eGFR <30 mL/min/1.73 m²  
• Discuss advanced care directive if dialysis inappropriate  
• Multidisciplinary team involvement | • 1–3 monthly clinical review  
• Assessment as for ‘orange’ clinical action plan |
functional status, life expectancy and health priorities. This is illustrated in the following case studies.

**Case study 1**
Brian, 71 years of age, a male nonsmoker, presents with several months of progressive lethargy. He has been treated for many years with perindopril 5 mg/day for hypertension but is otherwise well. On examination he is somewhat pale with a BP of 155/95 and heart rate of 78 bpm. Serum creatinine is elevated at 144 µmol/L; eGFR (42 mL/min/1.73 m²) and haemoglobin (103 g/L) are lowered. Fasting total cholesterol is raised: 6.5 mmol/L (HDL-cholesterol 0.9 mmol/L).

This case study highlights some important concepts. First, a relatively small increase in serum creatinine may actually represent a significant reduction in eGFR. Second, Brian has a high calculated cardiovascular risk of 25% over the next 5 years as per the Australian absolute cardiovascular disease risk calculator. Assuming the absence of other identifiable causes for anaemia such as occult blood loss, his fatigue is likely to be related to anaemia from cKD. While he does not meet Pharmaceutical benefits scheme criteria for erythropoietin replacement therapy, iron supplementation will still be of benefit. However, the focus of management in this patient should be investigation of the cause of renal impairment and aggressive control of cardiovascular risk factors.

**Case study 2**
June, 83 years of age, is a female nursing home resident with a 3 month history of lethargy, anorexia and itch. She has a longstanding history of type 2 diabetes mellitus, complicated by diabetic neuropathy and retinopathy, hypertension, hyperlipidaemia, osteoarthritis and a previous fractured neck of her left femur. Her medications include: metformin 2 g/day, rosuvastatin 5 mg/day, candesartan 16 mg/day, amlodipine 10 mg/day, paracetamol and glucosamine. Her lying and standing BP are 155/88 and 135/82 respectively, associated with some postural symptoms of dizziness. She has mild ankle oedema and her lung fields are clear to auscultation. Investigations reveal that her serum creatinine is elevated at 210 µmol/L, eGFR reduced at 18 mL/min/1.73 m² and she has macroalbuminuria (urinary ACR 52 mg/mmol). Other haematologic and biochemical parameters include: haemoglobin 92 g/L, potassium 5.9 mmol/L, urea 18 mmol/L, calcium 2.15 mmol/L, phosphate 1.90 mmol/L and HbA1c 7.1%. Six months prior, her eGFR was 22 mL/min/1.73 m².

In this case study, the patient is likely to have stage 4 cKD with macroalbuminuria due to a longstanding history of diabetes mellitus and hypertension. In addition to a postural BP drop, she is already at risk of falls due to significant comorbidities. Furthermore, there is some evidence to suggest that lower baseline systolic BP (≤130 mmHg) in individuals over 75 years of age is associated with increased mortality and cardiovascular hospitalisations.

### Table 3. Common causes of eGFR changes

| Reversible causes of eGFR decline | • Renal tract infection  
| • Fluid depletion  
| • Nephrotoxins  
| • Trimethoprim, cimetidine: cause a raised serum creatinine which does not reflect a true fall in GFR |
| Common causes of kidney disease in the elderly | • Type 2 diabetes  
| • Glomerulonephritis (eg. IgA nephropathy)  
| • Hypertension  
| • Polycystic kidney disease |

### Table 4. Medications and kidney disease

| Nephrotoxins in chronic kidney disease | • NSAIDs/COX-2 inhibitors  
| • ‘Triple whammy’ (NSAID, ACEI, diuretic)  
| • Lithium  
| • Aminoglycosides  
| • Radiographic contrast agents |
| Common medications that may need to be reduced in dose | • Antivirals  
| • Benzodiazepines  
| • Opioids  
| • Hypoglycaemic agents: metformin, sulfonylureas, gliptins  
| • Insulin  
| • Cardiac drugs: digoxin, sotalol, atenolol  
| • Thiazides, K+ sparing diuretics  
| • Low molecular weight heparins  
| • Psychotropics, anticonvulsants  
| • Antigout drugs: allopurinol, colchicine |

However, dialysis may be associated with only a limited survival benefit and an overall decline in functional status.

Conservative, nondialysis treatment of advanced CKD may therefore be a positive therapeutic option for elderly patients in whom dialysis is unlikely to prolong or improve quality of life. Elderly patients with a stable eGFR >30 mL/min/1.73 m², microalbuminuria and controlled BP can be managed successfully in the primary care setting.

### Patient focussed management

Management of CKD in many elderly patients should be more individualised rather than disease focussed, given the common interplay of complex comorbidities together with variability in functional status, life expectancy and health priorities. This is illustrated in the following case studies.
June's symptoms are likely to be related to advanced CKD, anaemia and hyperphosphataemia. Topical emollients, evening primrose oil and phosphate-binding therapy may be helpful in ameliorating pruritus. Metformin should be ceased given that her eGFR is <30 ml/min/1.73 m², and phosphate-binding therapy may be helpful in ameliorating pruritis.

and hyperphosphataemia. topical emollients, evening primrose oil

Key points
• CKD management is guided by staging through investigation of GFR, degree of albuminuria and aetiology.
• Appropriate control of hypertension, dyslipidaemia and glycaemia slow disease progression and reduce cardiovascular risk.
• Secondary complications of CKD may require careful monitoring with a multidisciplinary team.

Author
Richard KS Phoon FRACP, is Staff Specialist in Nephrology, Western Renal Service, Sydney, New South Wales, Honorary Tisher, the Australian and New Zealand Society of Nephrology and Chair, the Specialist Advisory Committee, Royal Australasian College of Physicians. rphoon@med.usyd.edu.au.

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References