Richard KS Phoon

Chronic kidney disease in the elderly

Assessment and management

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

CPD

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.[1,2] 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%.[3] 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 m^2 per decade.[4] 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 m^2.[5,6] 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.[7–9] Recent evidence suggests that even very elderly patients (>80 years of age) with modest reductions in eGFR (45–59 mL/min/1.73 m^2) have a higher prevalence of CKD-related complications compared to patients with an eGFR ≥60 mL/min/1.73 m^2.[10] Furthermore, as eGFR declines below 60 mL/min/1.73 m^2, there is an appreciable, increasing incidence of cardiovascular events and mortality.[11,12] As a result, age specific cut-points for CKD diagnosis and staging are not currently recommended.[13]

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.[14] People of Aboriginal or Torres Strait Islander origin may be screened from 30 years of age, as

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.[15] Testing for CKD should comprise a serum eGFR measurement, urinary albumin:creatine 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.[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.[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*.

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.[18–20] ACEI or ARB therapy may be effective, even in patients with severe CKD,[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.[22] By comparison, several studies demonstrate efficacy of combining

Table 1. Staging of chronic kidney disease[33]

		Kidney damage (as evidenced by albuminuria)		
Kidney function	**GFR (mL/min/1.73 m^2)**	**Normal (urine ACR mg/mmol) Male: <2.5 Female: <3.5**	**Microalbuminuria (urine ACR mg/mmol) Male: 2.5–25 Female: 3.5–35**	**Macroalbuminuria (urine ACR mg/mmol) Male: >25 Female: >35**
1	≥90	Not CKD unless haematuria, structural or pathological abnormalities present		
2	60–89			
3a	45–59			
3b	30–44			
4	15–29			
5	<15 or on dialysis			

ACEI or ARB monotherapy with other second-line agents, particularly thiazide diuretics and non-dihydropyridine calcium channel blockers.[23,24]

Blood pressure guidelines have recently been modified in view of recent evidence that does not support the use of lower targets.[25] Patients with CKD should maintain a BP that is consistently below 140/90 mmHg, although, if a patient has diabetes or microalbuminuria, a consistent BP below 130/80 mmHg is recommended.

Diabetes and dyslipidaemia

Intensive blood glucose control significantly reduces the risk of progression to proteinuria and overt nephropathy in patients with diabetes. A therapeutic target of HbA1c <7% and pre-prandial blood sugar levels of 4.0–6.0 mmol/L is advised, but must be applied with caution in especially frail individuals at higher risk of hypoglycaemia.

Chronic kidney disease is associated with abnormalities of lipid metabolism, especially in patients with proteinuria. In general, national cardiovascular targets of total cholesterol <4.0 mmol/L and LDL-cholesterol <2.5 mmol/L are advised.[26]

Anaemia, hyperparathyroidism and renal osteodystrophy

The prevalence of anaemia increases as GFR declines due to reduced erythropoietin production by the kidney and increasing resistance to its action due to hyperparathyroidism.

Iron deficiency is common in CKD and supplementation with oral or intravenous iron is required.[27] 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.[28] 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.

Table 2. Guidelines for the management of chronic kidney disease[33]

Colour code	Clinical action plan	Monitoring
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 m^2 • Discuss advanced care directive if dialysis inappropriate • Multidisciplinary team involvement	• 1–3 monthly clinical review • Assessment as for 'orange' clinical action plan

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[34]	
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[29] and an overall decline in functional status.[30]

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 m^2, 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.[31] 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 m^2) 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 m^2 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 m^2.

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.[32]

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 pruritis. Metformin should be ceased given that her eGFR is <30 mL/min/1.73 m^2, as she is at increased risk of lactic acidosis. Referral to a specialist renal service may give June a further opportunity to discuss her management goals, including advanced care directives and symptom management, with a multidisciplinary team. She would also benefit from erythropoietin replacement therapy. However, the GP may also be well placed to discuss with June her desires about future care.

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 Treasurer, the Australian and New Zealand Society of Nephrology and Chair, the Specialist Advisory Committee, Royal Australasian College of Physicians. rphoon@med.usyd.edu.au.

Conflict of interest: Richard Phoon has received payment from Baxter, Janssen, Novartis and Sanofi (consultancy); Amgen (grants); Baxter, Boehringer-Ingelheim and Novartis (lectures); and Roche and Shire (travel).

References

1. Australian Institute of Health and Welfare. An overview of chronic kidney disease in Australia, 2009. Canberra: AIHW, 2009.
2. Australian Institute of Health and Welfare. Chronic kidney disease hospitalisations in Australia 2000–01 to 2007–08. Canberra: AIHW, 2010.
3. Johnson DW. Evidence-based guide to slowing the progression of early renal insufficiency. Intern Med J 2004;34:50–7.
4. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis 2003;41:1–12.
5. Chadban SJ, Briganti EM, Kerr PG, et al. Prevalence of kidney damage in Australian adults: the AusDiab kidney study. J Am Soc Nephrol 2003;14(7 Suppl 2):S131–8.
6. White SL, Polkinghorne KR, Atkins RC, Chadban SJ. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Study GFR estimating equations: the AusDiab (Australian Diabetes, Obesity and Lifestyle) study. Am J Kidney Dis 2010;55:660–70.
7. Baggio B, Budakovic A, Perissinotto E, et al. Atherosclerotic risk factors and renal function in the elderly: the role of hyperfibrinogenaemia and smoking. Results from the Italian Longitudinal Study on Ageing (ILSA). Nephrol Dial Transplant 2005;20:114–23.
8. Fliser D, Franek E, Joest M, Block S, Mutschler E, Ritz E. Renal function in the elderly: impact of hypertension and cardiac function. Kidney Int 1997;51:1196–204.
9. Lindeman RD, Tobin J, Shock NW. Longitudinal studies on the rate of decline in renal function with age. J Am Geriatr Soc 1985;33:278–85.
10. Bowling CB, Inker LA, Gutierrez OM, et al. Age-specific associations of reduced estimated glomerular filtration rate with concurrent chronic kidney disease complications. Clin J Am Soc Nephrol 2011;6:2822–8.
11. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004;351:1296–305.
12. Keith DS, Nichols GA, Gullion CM, Brown JB, Smith DH. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. Arch Intern Med 2004;164:659–63.
13. Johnson DW, Jones GR, Mathew TH, et al. Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: new developments and revised recommendations. Med J Aust 2012;197:224–5.
14. Mathew TH, Corso O, Ludlow M, et al. Screening for chronic kidney disease in Australia: a pilot study in the community and workplace. Kidney Int 2010;77(S116):S9–16.
15. Australian Institute of Health and Welfare. Chronic kidney disease in Aboriginal and Torres Strait Islander people. Canberra: AIHW, 2011.
16. Johnson DW, Jones GR, Mathew TH, et al. Chronic kidney disease and measurement of albuminuria or proteinuria: a position statement. Med J Aust 2012;197:224–5.
17. Matsushita K, van der Velde M, Astor BC, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet 2010;375:2073–81.
18. Casas JP, Chua W, Loukogeorgakis S, et al. Effect of inhibitors of the renin-angiotensin system and other antihypertensive drugs on renal outcomes: systematic review and meta-analysis. Lancet 2005;366:2026–33.
19. Giatras I, Lau J, Levey AS. Effect of angiotensin-converting enzyme inhibitors on the progression of nondiabetic renal disease: a meta-analysis of randomized trials. Angiotensin-Converting-Enzyme Inhibition and Progressive Renal Disease Study Group. Ann Intern Med 1997;127:337–45.
20. Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345:851–60.
21. Hou FF, Zhang X, Zhang GH, et al. Efficacy and safety of benazepril for advanced chronic renal insufficiency. N Engl J Med 2006;354:131–40.
22. Yusuf S, Teo KK, Pogue J, et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008;358:1547–59.
23. Bakris GL, Sarafidis PA, Weir MR, et al. Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (ACCOMPLISH): a prespecified secondary analysis of a randomised controlled trial. Lancet 2010;375:1173–81.
24. Bakris GL, Toto RD, McCullough PA, Rocha R, Purkayastha D, Davis P. Effects of different ACE inhibitor combinations on albuminuria: results of the GUARD study. Kidney Int 2008;73:1303–9.
25. Upadhyay A, Earley A, Haynes SM, Uhlig K. Systematic review: blood pressure target in chronic kidney disease and proteinuria as an effect modifier. Ann Intern Med 2011;154:541–8.
26. Diabetes Australia. Diabetes management in general practice. 17th edn, 2011.
27. Gotloib L, Silverberg D, Fudin R, Shostak A. Iron deficiency is a common cause of anemia in chronic kidney disease and can often be corrected with intravenous iron. J Nephrol 2006;19:161–7.
28. Kandula P, Dobre M, Schold JD, Schreiber MJ Jr, Mehrotra R, Navaneethan SD. Vitamin D supplementation in chronic kidney disease: a systematic review and meta-analysis of observational studies and randomized controlled trials. Clin J Am Soc Nephrol 2011;6:50–62.
29. Chandna SM, Da Silva-Gane M, Marshall C, Warwicker P, Greenwood RN, Farrington K. Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. Nephrol Dial Transplant 2011;26:1608–14.
30. Kurella Tamura M, Covinsky KE, Chertow GM, Yaffe K, Landefeld CS, McCulloch CE. Functional status of elderly adults before and after initiation of dialysis. N Engl J Med 2009;361:1539–47.
31. Bowling CB, O'Hare AM. Managing older adults with CKD: individualized versus disease-based approaches. Am J Kidney Dis 2012;59:293–302.
32. Weiss JW, Johnson ES, Petrik A, Smith DH, Yang X, Thorp ML. Systolic blood pressure and mortality among older community-dwelling adults with CKD. Am J Kidney Dis 2010;56:1062–71.
33. Kidney Health Australia. Chronic disease management in general practice. 2nd edn, 2012. Available at www.kidney.org.au/LinkClick.aspx?fileticket=sMKP3HBuquM%3d&tabid=635&mid=1584.
34. Faull R. Lee L. Prescribing in renal disease. Aust Prescr 2007;30:17–20.

correspondence **afp@racgp.org.au**