Management of chronic kidney disease

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Abstract

Management of chronic kidney disease (CKD) requires a systematic approach that includes all components of the chronic disease model. National guidelines are now available for the identification, management and referral of CKD. Some causes of CKD require specific additional management directed at the underlying cause. For many patients, control of cardiovascular risk factors is the most important intervention, as these risk factors also promote progressive loss of kidney function. More intensive reduction of blood pressure and/or the use of inhibitors of the renin/angiotensin axis are recommended in the treatment of proteinuric kidney disease, including diabetic nephropathy. In these patients, treatment should be adjusted to achieve maximum reduction of urine protein excretion. Dietary salt restriction is an important adjunct to drug therapy. Smoking cessation, obesity correction, lipid-lowering treatment and (among patients with diabetes mellitus) glycaemic control are also important. The dosage of drugs that are cleared by the kidney should be adjusted, and care must be taken to avoid nephrotoxic drugs. Acute hypovolaemia and hypotension can further damage kidney function and should be avoided, or treated promptly. Patients with CKD require lifelong follow-up; this can commonly be achieved most efficiently in the primary care setting. Symptoms are common only in advanced CKD. Patients likely to progress to established renal failure should be referred early enough to allow adequate preparation for renal replacement therapy.

Keywords antihypertensive therapy; chronic disease management; chronic kidney disease; glomerulonephritis; progression

Principles of chronic disease management

Chronic kidney disease (CKD) is a prime example of a chronic disease requiring life-long management, involving the patient, the primary care team and specialists. Most people with CKD also have other long-term conditions (hypertension, cardiovascular disease, diabetes mellitus, atherosclerosis). Current disease-based clinical services (e.g. nephrology clinics, hypertension clinics, diabetes clinics, heart failure clinics) seldom provide optimal care, with poor communication occurring between these 'silos' of care, and between hospital-based clinics, the primary care team, and the patient. This lack of integration is harmful and can contribute to patients' loss of control, and to conflicting messages on what drug treatment the patient should be taking. The system is also wasteful, with much duplication of effort, tests, and wasted travel time. Research on systematic attempts to achieve improvement in the delivery of care for patients with chronic diseases has resulted in development of a framework, the 'chronic care model'. Improvement is more likely if each component of the organization of care (self-management; decision support; delivery system design; clinical information systems) is addressed, and unlikely if, for instance, improvement efforts are confined to a hospital-based clinic.[1,2] Many of the components of the model, including national guidelines on identification, management, and referral, are already in place for CKD.[3]

Early CKD is largely asymptomatic, so a balance has to be struck between 'labelling' patients as having 'chronic kidney disease' and ensuring that patients who are at increased risk of cardiovascular disease or progressive loss of kidney function are identified and offered the options of treatment that will reduce these risks.

Diagnosis of chronic kidney disease

In this article, CKD will be defined according to the five-stage classification adopted in the UK (see Table 1 in *Epidemiology and Causes of Chronic Kidney Disease* on page 402 of this issue).[3,4] This classification endorses use of the four-variable Modification of Diet in Renal Disease (MDRD) equation to estimate normalized glomerular filtration rate (GFR) from serum creatinine, age, gender, and racial origin. The estimate provided by the laboratory should be used wherever possible, as this should include correction factors for the type of creatinine assay used (see *Medicine* 2011; **39(6):** 306–311).[4,5]

Some patients will have other evidence of chronic kidney damage, such as:

- persistent microalbuminuria;
- persistent proteinuria;
- persistent haematuria (after exclusion of other causes, e.g. urological disease);
- structural abnormalities of the kidneys demonstrated on ultrasound scanning or other radiological tests (e.g. polycystic kidney disease, reflux nephropathy); or
- biopsy-proven chronic glomerulonephritis (most of these patients will have microalbuminuria or proteinuria, and/or haematuria).

In February 2007, a consensus conference in the UK[6] approved two enhancements to this five-stage classification; dividing stage 3 CKD into stage 3A (eGFR 45–59) and stage 3B (eGFR 30–44), and adding the suffix 'p' to the GFR-based stage for patients with proteinuria (random urine protein:creatinine ratio >100 mg/mmol). These changes are endorsed by the National Institute for Health and Clinical Excellence (NICE),[4] the Scottish Intercollegiate Guidelines Network (SIGN)[7] and the American National Kidney Framework's National Kidney Foundation Kidney Disease Outcome Quality Initiative (KDOQI) guidelines.[8]

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Approach to common symptoms in chronic kidney disease

Symptom	Cause	Intervention
Nocturia	Reduced ability to produce concentrated urine	No specific treatment available. If the patient is taking diuretics, ensure that these are taken in divided doses in the morning and late afternoon. Fluid overload and systemic hypertension may also contribute to nocturia, and should be fully corrected
Pruritus	Dry skin; histamine release; phosphate accumulation may also play a role	Skin hydration; antihistamines; treatment of hyperphosphataemia. Correction of anaemia is also of benefit
Restless leg syndrome	Uncertain	Exclude iron deficiency. Drug treatment with antiparkinsonian drugs, gabapentin, codeine, or clonazepam may help individual patients (all unlicensed indications)
Loss of appetite, nausea, and vomiting	Uncertain — accumulation of uraemic metabolites	Renal replacement therapy (RRT). If an active decision has been made not to embark on RRT, anti-emetics may be used
Neuropathy	Uncertain — accumulation of uraemic metabolites	Beware attributing clinically evident neuropathy to chronic kidney disease (CKD), particularly in stage 1–4; consider alternative causes. Although patients with advanced CKD often have subclinical evidence of impaired peripheral nerve function, this is seldom severe

Table 1

Proteinuria should be assessed by measurement of either the urinary protein:creatinine or albumin:creatinine ratio.[9] Adoption of this enhanced classification system is likely to focus greater attention on those patients in stage 3 CKD, who are at greatest risk of complications of CKD and progressive loss of kidney function.

Limitations of MDRD and the CKD-EPI formula

There are many limitations to the use of the MDRD formula to estimate renal function. First, the formula is less accurate when the GFR is more than 60 ml/minute/1.73 m^2. Second, its use has not been fully validated in the elderly, children or pregnant women, acute kidney injury (AKI), extremes of body size, or in ethnic groups other than Caucasians and African-Americans. There is therefore ongoing work to find a more accurate estimation of renal function than that offered by the MDRD; as a result, the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula was published in May 2009. Preliminary work suggests that the CKD-EPI equation performs better (with less bias and greater accuracy) than the MDRD formula, especially at higher GFRs, but it has not been extensively validated in the elderly or in ethnic minorities. The formula is more complex to compute than the MDRD formula, and has not yet been adopted by UK laboratories for routine reporting of eGFR.

Specific causes of CKD

Some cases of CKD are attributable to specific diseases, for which specific treatments are sometimes available to reduce the risk of progressive kidney damage. However, most patients with these well-defined causes of CKD will also benefit from the non-specific interventions discussed below.

Non-specific causes of CKD

Many patients with reduced GFR do not have proteinuria, radiological abnormalities or other markers that suggest a specific underlying cause; in particular, elderly patients with reduced GFR commonly have no proteinuria.[10] There is controversy about the assessment of renal function in the elderly and how renal function changes as part of 'normal ageing'.[11]

The MDRD formula is not as well validated in the elderly, and any creatinine-based formula that incorporates assumptions about muscle mass at different ages will face the same problems. The apparent high prevalence of CKD in the elderly may occur because of:

- the presence of numerous risk factors for CKD, such as diabetes and hypertension;
- an age-associated decline in kidney function that is not explained by other known risk factors; or
- inaccuracy of creatinine-based estimating equations in the elderly population.

The Baltimore Longitudinal Study of Aging (BLSA) suggested that on average kidney function tends to decline with age even without comorbidities, but this decline did not appear to be inevitable.[12]

The majority of CKD in the elderly is non-progressive and research is needed to identify those at risk of developing established renal failure. The increased relative risk for death associated with lower GFR (mostly due to cardiovascular disease) is more evident in younger people than in older people, largely because of fewer competing risks in younger people; patients aged over 75 years with moderate eGFR 45–60 ml/minute/1.73 m^2 were at no higher risk of death over 1–3 years follow-up than their age peers with levels of eGFR above 60 ml/minute/1.73 m^2.[13]

Reducing the risk of progressive loss of GFR

In addition to specific therapy targeted at the underlying primary disease, recognition of the role of several modifiable secondary factors associated with progressive kidney damage is important clinically, as these can be treated effectively thereby minimizing renal injury. Most of these interventions also reduce the risk of cardiovascular disease (see *Cardiovascular Complications of Chronic Renal Disease* on pp 421–424 of this issue).